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Neither Benign nor Self-limited: A Nearly Fatal Case of Henoch-Schönlein Purpura

First Author: Dylan Norton, BA Second Author: Mark Reid, MD

Introduction: Henoch-Schönlein Purpura (HSP) is a systemic IgA vasculitis characterized by palpable purpura, arthralgia, nephropathy, and abdominal symptoms. It is generally a self-limiting disease, but corticosteroids and IVlg may be needed in severe cases. Steroid treatment can result in significant immunosuppression, leaving patients at risk for opportunistic infections, including cytomegalovirus (CMV). Although HSP generally affects children, about 10% of cases occur in adults, and may be severe. Significant renal involvement is more common in adults, and thrombotic vasculitic lesions of the small intestine may cause infarction and bowel necrosis. Fatalities have been reported. Nearly all adults have been exposed to CMV and have anti-CMV antibodies. CMV persists in many tissues, however, and may reactivate and cause severe disease in immunocompromised patients. CMV is thought to be more likely to activate in areas of focal inflammation. CMV proliferation has been reported to complicate HSP on occasion, resulting in serious sequelae.

Case Description: A 32 year-old man with a past medical history of pustular psoriasis and recent prednisone therapy for a psoriasis flare presented with diffuse abdominal pain, nausea, vomiting, and loose stools. Skin exam revealed psoriatic lesions. The patient was afebrile. Laboratory findings were within normal limits with the exception of a significant leukocytosis. A CT scan of the abdomen showed terminal ileitis. The most likely diagnosis at the time was thought to be inflammatory bowel disease. While awaiting colonoscopy, the patient developed abdominal distention, fever, and peritonitis. He was taken to surgery, revealing a focal necrotic segment of jejunum. Post surgically, palpable purpura was noted on his lower extremities bilaterally. Biopsy of the lesions demonstrated a leukocytoclastic vasculitis consistent with HSP, and high-dose prednisone was begun. Endoscopy was performed, revealing inflammation of the duodenal lamina propria with CMV viral inclusions. Ganciclovir was commenced.

The patient developed acute GI hemorrhage, requiring a massive transfusion of over 100 units of packed red blood cells. Multiple embolizations by interventional radiology failed to achieve hemostasis. An emergent surgical resection of the small bowel was performed and bleeding was finally controlled. He eventually recovered. He will require life-long TPN, and a small-bowel transplant has been considered.

Discussion: Although rare in adults, HSP can be a life-threatening cause of abdominal pain that may be difficult to diagnose. The classic purpuric skin lesions usually precede abdominal involvement, but may not occur until later in the disease course. CMV enteritis is seen in patients receiving chronic immunosuppressive therapy or with immune deficiencies, especially those receiving chemotherapy or high-dose steroids. There should be a high index of suspicion for CMV infection in susceptible patients. Symptoms are non-specific, yet early detection and treatment with ganciclovir is critical. Advanced disease may require extensive surgical resection, in addition to medical therapy.
Acquired factor inhibitors are rare coagulopathies, of which factor VIII inhibitor or acquired hemophilia A is the most common. Bleeding is the most common manifestation and often constitutes a medical emergency with mortality rates as high as 22% from directly and indirectly related complications. Should an internist suspect hemophilia A, an urgent hematology consultation is recommended to mitigate these complications.

A 74-year-old female with a history of rheumatoid arthritis and hypothyroidism presented to her primary care physician with painful muscular swelling, bruising and fatigue for 2 weeks. She first noted right inner arm swelling that bruised and subsequently developed left arm swelling and right calf swelling which progressively extended up her right thigh and down her left leg. She denied trauma or similar episodes previously. She had undergone prior surgeries without transfusion and had no family history of bleeding. She denied using NSAIDs, aspirin or warfarin. Physical examination revealed conjunctival pallor with significant swelling and large ecchymoses on all extremities. Initial labs revealed normocytic anemia with hemoglobin of 10.5. The next day she felt worse, presenting to the ER with a hemoglobin of 8.5, reticulocytosis and an elevated creatine kinase. Coagulation studies revealed a normal protime (PT) of 13.7 and normal fibrinogen activity but an elevated partial thrombin time (PTT) of 118. She required admission with hematology consultation. No lupus anticoagulant was detected. A 1:1 mixing study revealed a factor inhibitor, prompting transfusion of 2 units of cryoprecipitate. Further testing revealed adequate VWF activity and factor VIII activity of 50 and malignancy.

So if an elderly patient with this background presents with acute onset hematomas, ecchymoses, and no history of coagulopathy or trauma, the presence of an acquired factor inhibitor should be suspected. Diagnosis is supported by a solitary prolonged PTT that fails to correct on mixing with normal plasma. Invasive diagnostic procedures and intramuscular injections should be avoided due to bleeding risk. Acutely, inhibitors of low titer are treated with factor VIII concentrates or DDAVP, while higher titers often require activated prothrombin complexes such as FEIBA. Long term management aims to eliminate the inhibitor through immunosuppressive medications including prednisone, cyclophosphamide and rituximab.
ILLINOIS PODIUM PRESENTATION - CLINICAL VIGNETTE Xavier Pereira

Should we revisit our guidelines for antibiotic prophylaxis before endoscopic procedures in patients with prosthetic valve?

First Author: Xavier Pereira, Swarup Kumar, Karthik Ragunathan, Teresa Lynch

A 71-year-old Caucasian male with a history of hypertension and mechanical aortic valve replacement presented to the emergency room for altered mental status. The patient had episodes of confusion, troubled speech, and left sided hemiparesis. He and his wife denied fevers, chills, fatigue or any other symptoms in the previous weeks. His home medications included Amlodipine, Labetalol and Warfarin. The patient had recently stopped Warfarin and was taking Enoxaparin due to an elective screening colonoscopy 14 days prior to presentation. During this procedure he had multiple polypectomies of tubulovillous adenomas that ranged from 0.5 – 2.5 cm in size.

On initial examination the patient was alert and oriented to person, place but not time. Neurological exam was significant for left-sided hemianopsia, weakness, dysmetria, and hemianesthesia. The rest of the physical exam was normal. Laboratory studies were significant for an INR of 1.8 sec (0.8 – 1.2), PTT of 35 sec (24 – 33) and a normal complete metabolic profile. CT of the brain showed subacute ischemic infarcts in the right parietal and left occipital lobes and the patient was admitted for stroke management. Given his history of a mechanical valve he underwent a transthoracic echocardiogram but the prosthetic valve was not well visualized. Additionally, routine blood cultures drawn on admission grew gram-positive cocci in pairs. Therefore, given a high index of suspicion for infective endocarditis from his prosthetic valve, a trans-esophageal echocardiogram was done and showed multiple small mobile echodensities that were consistent with thrombi. Blood cultures grew Enterococcus faecalis and Vancomycin and Gentamycin were started. E. Faecalis is normal bowel flora suggesting that his bacteremia likely stemmed from his recent colonoscopy. He had no antibiotic prophylaxis prior to the procedure.

Antimicrobial prophylaxis for bacterial infective endocarditis (IE) is a controversial issue. The lifetime risk of IE increases thrice for patients who have had prior prosthetic valve endocarditis. The 2007 ACC/AHA guidelines do not consider any gastrointestinal (GI) endoscopic procedures as a risk factor for IE and do not recommend routine use of prophylaxis, even in patients with prosthetic valves. Similarly, the 2008 American Society for Gastrointestinal Endoscopy (ASGE) does not recommend prophylaxis for patients with any cardiac conditions undergoing GI procedures. Incidental case reports have described IE in patients following endoscopic procedures similar to our case scenario; however, the absolute risk of this association remains uncertain. The risk of bacteremia following colonoscopy is estimated to be between 4 and 25%. Whether these patients with prosthetic valves need to be covered with prophylactic antibiotics prior to endoscopy should be addressed with randomized studies to prevent IE.
TENNESSEE PODIUM PRESENTATION - CLINICAL VIGNETTE Andrew W Hahn

An Unexpected Killer, Spontaneous Hemoperitoneum

Andrew Hahn Rebekah Mulligan Sara Powell Brice Zogleman

Spontaneous hemoperitoneum is a rare cause of atraumatic intraperitoneal hemorrhage that has life threatening implications if the diagnosis is delayed.

The patient is a 68 year-old male with a past medical history significant for alcoholic cirrhosis with portal hypertension and cerebrovascular accident for which he was taking clopidogrel. He was sent to the ED for evaluation of a decreasing hemoglobin; in addition, the patient endorsed a productive cough and abdominal pain. Review of systems was otherwise negative. He was admitted in the month prior for health-care associated pneumonia (HCAP).

Initial evaluation revealed a male in no acute distress with stable vital signs. Physical examination revealed diminished breath sounds at bilateral bases, a soft abdomen with no tenderness to palpation or peritoneal signs, and a normal rectal exam with negative stool guaiac. While decreased from his baseline hemoglobin of ~11 g/dL, his hemoglobin was stable from his admission one month prior at 7.6 g/dL. His platelet count on admission was 58 having trended down from 100 three months prior to admission. A CT chest noted consolidation of the right lower lobe consistent with pneumonia. Other findings included trace ascites with signs of cirrhosis.

The patient was admitted for failure of outpatient treatment of HCAP. Clopidogrel was held due to his hemoglobin, and he was transfused one unit of packed red blood cells. Gastroenterology deferred colonoscopy until outpatient. On hospital day 7, the patient’s pneumonia was improving, yet he became tachycardic at 118 BPM with a stable blood pressure. That evening, the patient was found on the floor of his bathroom unresponsive. Resuscitation efforts were unsuccessful, and the patient died.

An autopsy was performed that showed right lung consolidation consistent with HCAP. Additionally, 1.5 L of blood was found in the peritoneal cavity without evidence of perforated visceral organs, microscopically damaged vasculature, or injury to spleen or kidney parenchyma. Incidentally, a myocardial infarction was noted to have occurred 5 to 7 days prior to death, despite the patient never complaining of chest pain. The pathologist hypothesized that the intraperitoneal hemorrhage led to hypotension that superimposed with his recent subacute myocardial infarction led to the syncopal event and death.

Spontaneous hemoperitoneum is the presence of blood within the peritoneal cavity without preceding trauma. Blood is a mild peritoneal irritant, so the symptoms can vary and diagnosis often relies upon imaging, specifically CT. While the etiology can include any visceral organ or vessel, a patient’s age and co-morbidities often point towards the cause. Since the natural course of spontaneous hemoperitoneum is fatal, prompt diagnosis and surgical intervention is essential for patient survival.
Beyond Typhoid Mary: The Sophistication of Salmonella typhi

First Author: Charis Santini, Second Authors: Curtis R Mirkes, DO FACP, Cedric Spak, MD

Introduction: Though typhoid fever is a substantial global concern (10-100 cases per 100,000 people yearly), the incidence of S. typhi infection in the United States is only 200-300 reported cases per year. As resistant strains are increasing worldwide, a clinician in the United States may find treating typhoid fever in returning travelers more difficult. S. typhi needs to be on the differential diagnosis for clinicians to ensure appropriate treatment. This case demonstrates the variability within which typhoid fever can present; with cyclical fevers more suggestive of malaria, and myalgia with headache more suggestive of dengue fever.

Discussion: A 20 year-old formerly healthy male presented with an 18 day history of intermittent fever and myalgia. The fever spikes to approximately 104°F in the late afternoons. Associated symptoms include: chills, headache, weakness, nausea/vomiting, and occasional loose stools. The patient returned from Bangladesh five days prior to symptom onset. He denied contact with contaminated food, sick contacts, bloody diarrhea, constipation, or rashes. Initial vitals consisted of a temperature of 103°F, blood pressure of 125/71 mmHg, pulse of 105 per minute, and a respiratory rate of 20 per minute. Physical exam was noncontributory except for a systolic flow murmur. Labs were significant for a WBC of 4.7 with 37% bands, thrombocytopenia (109 x10^3/L), hyponatremia (129 mmol/L), and elevated transaminases (AST/ALT: 157/138 U/L). Cultures were obtained and the patient was placed empirically on vancomycin and zosyn. Serum cultures were positive after 48 hrs. for gram negative rods. After three days of treatment, the patient’s symptoms did not improve. The patient’s liver transaminases continued to increase to a max AST/ALT of 301/245 U/L. Also, his H&H dropped with labs consistent with intravascular hemolysis. The patient’s symptoms and labs improved on ceftriaxone. Culture growth further revealed S. typhi group D with intermediate sensitivity to ciprofloxacin. He was discharged on oral antibiotics.

Conclusion: Fever of unknown origin in returning travelers reminds physicians to maintain a relevant third-world differential diagnosis. Hepatomegaly and elevated liver enzymes can be appreciated in typhoid fever with serum transaminases less than 1,000 U/L. This case, however, was not merely the straight forward picture of enteritis, bloody diarrhea/constipation, and salmon-colored macules a student is taught to expect. Intermittent fevers with possible hemolysis could be consistent with malaria. Once typhoid fever is diagnosed, a new difficulty arises with the changing resistance patterns; selecting appropriate antibiotic therapy is of most importance. Fluoroquinolones for 7-10 days is the recommended treatment. However, in certain regions, including South Asia, fluoroquinolone resistance is becoming more prevalent. Therefore, in cases of known fluoroquinolone resistance recommendations promote the use of a third generation cephalosporin or azithromycin. Delaying appropriate therapy increases the risk of relapse and can result in 10-20% mortality rates.
STUDENT VIGNETTE POSTER FINALISTS
ARIZONA POSTER FINALIST - CLINICAL VIGNETTE James Lish

Miliary tuberculosis disguised as epididymo-orchitis

First Author: James Lish Bassam Hattab MD Venuu Gupta MD Steve Kaplan MD Mohanad Al-Qaisi MD

A 40 year old male with no past medical history was diagnosed with epididymo-orchitis and started on oral antibiotics after presenting to his primary care provider with right side testicular pain and swelling. Two months later the patient presented to the emergency department with worsening pain, fatigue, fevers, headaches, nausea, vomiting, and a 40-pound unintentional weight loss.

On initial physical exam, a tender cystic mass overlying the distal epididymis was palpated. Neurological exam exhibited left sided spinal accessory nerve weakness, mild left side facial droop, and staggering on heal-to-toe gait. Testicular ultrasound showed an enlarged right testicle and epididymis, with increased vascularity and heterogeneity, and a 2 x 3 cm complicated fluid collection inferior to the right testicle. Laboratory studies were remarkable for a normal WBC, low serum sodium, decreased serum osmolality, and increased urine osmolality.

Patient was admitted for hyponatremia secondary to SIADH and Urology was consulted for surgical evaluation. The following day, the patient underwent right sided orchiectomy and scrotal abscess incision and debridement. His hyponatremia was gradually corrected with free water restriction while a cause for the SIADH, and other symptoms, was investigated. Chest CT revealed diffuse interstitial micro nodularity and several densely calcified mediastinal lymph nodes. Brain CT showed small 5-7 mm rim-enhancing lesions involving the cerebellum bilaterally. Subsequent Brain MRI revealed numerous ring-enhancing lesions throughout the cerebellum and supratentorial brain, as well as acute infarcts within the left cerebellum and right putamen/posterior limb internal capsule. An echocardiogram was normal.

Meanwhile, the patient remained hemodynamically and neurologically stable, only complaining of moderate headaches and intermittent fevers. The following day, testicular pathology showed necrotizing, granulomatous epididymo-orchitis involving the spermatic cord with positive stain and culture for acid-fast bacilli (AFB). A QuantiFERON-TB level was positive, and the patient was isolated and started on anti-TB therapy with high dose steroids for presumed CNS involvement. Lumbar puncture revealed an elevated protein, normal glucose, and increased neutrophils consistent with an early tuberculous meningitis. All remaining cultures, tumor markers and labs, including HIV and other STIs, were unremarkable.

The patient was found to have no active pulmonary TB, and careful history revealed no source of exposure. He was subsequently discharged home under close follow up with public health department. A diagnosis of miliary TB, as supported by pathology, adequately explains the genitourinary, electrolyte, pulmonary and CNS abnormalities seen in this patient. Furthermore, this case illustrates that miliary TB can occur in otherwise healthy individuals and can present as epididymo-orchitis with SIADH.
CALIFORNIA POSTER FINALIST - CLINICAL VIGNETTE Tanya Doctorian

Differentiating Constrictive Pericarditis from Restrictive Cardiomyopathy as a Cause of Right Heart Failure: A Clinical Vignette

Tanya Doctorian, Gaurav Tyagi, MD, David Rabkin, MD, Anthony Hilliard, MD

Constrictive pericarditis (CP) is characterized by a rigid, noncompliant pericardium that prevents adequate diastolic filling of the ventricles and can result in diastolic heart failure and often presents with nonspecific symptoms and/or findings consistent with right heart failure. Differentiation between CP and restrictive cardiomyopathy, another cause of diastolic heart failure, is critical as pericardiectomy is curative for CP whereas open heart surgery has no role in treating other causes of restrictive heart failure. This distinction is often difficult on clinical grounds alone but is suggestive on comprehensive echocardiography—a tool which is often used as the initial screening imaging modality.

This is a 43-year-old man with a history of diabetes, morbid obesity, tobacco use and renal insufficiency, who presented with a 6 month history of several admissions for acute on chronic shortness of breath, fatigue and fluid retention. He denied a history of radiation, chest trauma, steroid use, cardiovascular surgery, or prior known infection. Physical exam showed marked volume overload, bibasilar rales, 1-2/6 holosystolic murmur at the left lower sternal border, and S3 at the LV apex. Body habitus made JVP assessment difficult. The extremities showed 4+ edema. Chest x-ray showed mild pulmonary edema, normal-sized cardiac silhouette sign and a calcified pericardium.

Due to the patient’s body habitus, no features suggestive of constrictive pericarditis were discernable on transthoracic echocardiography. Given that CP was still on the differential, he underwent hemodynamic cardiac catheterization. Right heart catheterization demonstrated a characteristic “square-root sign”, severely elevated filling pressures, and equalization of diastolic pressures in all four chambers, which can be consistent with either restrictive cardiomyopathy or constrictive pericarditis. Thus, simultaneous left ventricular and pulmonary capillary wedge pressures and left and right ventricular pressures were obtained. The pressures showed dissociation of intrathoracic and intracardiac pressures with inspiration and enhanced ventricular interdependence. In addition, severe pericardial calcification and epicardial fixation of all three coronary arteries were noted on fluoroscopy and angiography. These findings are consistent with CP.

The patient underwent pericardiectomy. Intra-operative findings were consistent with CP—the pericardium was rigid and adherent to the surface of the heart. During his post-operative stay, the patient had a 40 kg diuresis. Pathologic analysis of the pericardium revealed the possibility of parvovirus as a rare, and previously, unreported cause of CP in an adult. When formulating a patient’s differential diagnosis of volume overload and right heart failure it is critical to include the diagnosis of CP as part of that differential as its treatment is vastly different (pericardiectomy) from other causes within that differential. When screening tests such as echocardiography cannot adequately exclude the diagnosis of CP, invasive hemodynamic testing is necessary to establish or refute the diagnosis of CP. The present case illustrates this point.
CALIFORNIA POSTER FINALIST - CLINICAL VIGNETTE Fady El-Gabalawy

Sorry to Burst Your Bubble: It’s an Emergency!

Fady El-Gabalawy, MS4 and Brian Kwan, MD

Introduction: Infected arterial aneurysms may be due to:

- Direct bacterial inoculation (e.g. IVDA)
- Bacteremic seeding of preexisting aneurysms or atherosclerotic plaques
- Septic embolization (e.g. endocarditis)
- Extension of a contiguous infection

Most common pathogens implicated are Staphylococcus and Salmonella species. Morbidity is high and management is highly dependent on the cause, location, and patient comorbidities. Treatment generally consists of antibiotics and surgical debridement with vascular reconstruction if possible

Case Presentation: 63 year old Caucasian male with history of uncontrolled diabetes presents with 4 weeks of worsening back pain and lower urinary tract symptoms. He was diagnosed and treated at an outside hospital 2 weeks prior for Klebsiella urinary tract infection. In the ER, his vitals were significant for fever to 102° F. On physical exam, he had mild abdominal tenderness without rebound or guarding and mild lumbar spinal tenderness. Initial labs were remarkable for a WBC of 10.6 K/uL with 79.8% S and 12.5 %L, hemoglobin of 8.4 g/dl (baseline HgB of 9.5), glucose of 457 mg/dl, and a CRP of 23.96 mg/dl (normal range 0 - 0.30). Chest X-ray and urinalysis were unremarkable.

Hospital Course: Aerobic and anaerobic blood cultures drawn on admission quickly grew a Klebsiella pneumoniae isolate. CT of the abdomen demonstrated:

- A large gas-containing retroperitoneal abscess extending from the level of the dome of the liver inferiorly to the superior margin of L4
- A thin and irregularly walled 2.8 cm right aortic aneurysm at the L2-L3 that appeared to be at high risk of rupture
- Suggestion of vertebral osteomyelitis at the L2-3 level in contiguity with the abscess, which was later confirmed by MRI

Vascular and General Surgery, Interventional Radiology (IR), and Infectious Disease were emergently consulted. Treatment was narrowed to Gentamycin and Ceftriaxone based on sensitivities. The large amount of gas in the abscess suggested a fistulous connection with the duodenum, but there was no evidence of this on preoperative endoscopy. Vascular surgery performed an endovascular repair of the aortic aneurysm, and IR subsequently attempted drainage of the pre-vertebral abscess, but it persisted. The patient returned to the Operating Room for open washout and debridement of the abscess. Intraoperatively, it was noted that the aorta had eroded to the level of the endograft, which was now exposed to the abscess cavity. Post-op course was complicated by ATN, which improved with discontinuation of Gentamycin. The patient was discharged home on 6 total weeks of IV Ceftriaxone.
Discussion: The patient likely developed the infected aneurysm via direct extension of his vertebral osteomyelitis and associated prevertebral abscess into the aortic wall. The same isolate of Klebsiella pneumoniae was implicated in the patient’s earlier UTI as well as his vertebral osteomyelitis. This may have occurred via bacteremia or seeding from Batson’s venous plexus (cerebrospinal venous system), a valveless system located in the epidural space which drains the pelvis (including the bladder) and extends the length of the vertebral column. Klebsiella is a very unusual cause of infected aneurysm, but a number of cases, particularly from East Asia, Taiwan, and Japan have been described. Uncontrolled diabetes was a risk factor in almost all cases.
Suntan, Syncope, and Schmidt Syndrome

First Author: Nadin Faidi

Introduction: Autoimmune polyendocrine syndrome type 2 (APS II)- also known as Schmidt Syndrome- is a group of endocrinopathies in which at least 2 systems are involved. With an incidence of 1.4-2 per 100,000 and women being affected three times more than men, it is no wonder that the diagnosis of APS II can be overlooked in a male college student. Below is a case of AP II initially presenting as syncope secondary to adrenal insufficiency.

Case Description: An 18 year old Caucasian male presented to the Emergency department after he collapsed and lost consciousness for a few minutes upon getting out of bed. The patient denied having experienced prior episodes of syncope. Medical history, family history, and physical exam were unremarkable. Review of systems was impressive for nausea and lightheadedness before and after syncope. EKG and Chest X-ray were WNL. Laboratory results in the ER showed a serum sodium 131 mmol/L, glucose 62, TSH 10.56, Free T4 1.21. After correction of electrolyte abnormalities and a diagnosis of vasovagal syncope, this patient was discharged and to receive further evaluation with an endocrinologist. Follow up laboratory testing 3 weeks later revealed serum AM cortisol .8 mcg/dl, ACTH 1540 pg/ml, and prolactin 41. With a high index of suspicion for primary adrenal insufficiency, further questioning revealed a 6-month history of darkening of the skin that did not fade, a 24-pound weight loss and progressive fatigue over 8 months. This constellation of symptoms and laboratory findings were consistent with a diagnosis of APS II involving Hashimoto’s Thyroiditis and Addison’s disease. The patient was educated about his condition, instructed to take daily Hydrocortisone and Fludrocortisone, Thyroxine, and to wear a medical alert bracelet.

Discussion: The workup for syncope is vast, and adrenal insufficiency is not commonly sought out as an explanation for it. On first impression, it may have been easy to attribute this young Caucasian man’s bronzed appearance to the California sun. But what were we to make of his hypothyroidism? Studies have shown that only 1% of patients with thyroid disease will develop adrenal insufficiency, and that therefore, routine screening for other autoimmune diseases is not cost effective. This case illustrates that in a patient presenting with syncope, a thorough history is crucial in order to delineate resources effectively to establish the underlying pathology. Adrenal insufficiency can be life threatening and prompt recognition is crucial. Thus, in the setting of syncope, Hashimoto’s Thyroiditis, and a suntan that does not fade, further assessment for concomitant autoimmune disorders should be pursued, as demonstrated by this unusual presentation of APS II.
Disseminated tuberculosis

Nadia Guardado MS, Pouria Kashkouli MD

Disseminated tuberculosis is a clinical disease caused by hematogenous propagation of Mycobacterium tuberculosis. It is fatal if left untreated. In 2013, 9 million new cases of tuberculosis were reported worldwide, compared to 9,582 total new cases in the US, of which 21% were disseminated tuberculosis. The rarity of tuberculosis in the US and the nonspecific nature of presentation of disseminated tuberculosis makes its diagnosis challenging.

A 71-year-old woman born and raised in the Philippines with a history of living-donor renal transplant and diverticulosis was admitted to the hospital because of a 5-day history of fever and debilitating weakness. Two months prior to presentation, she began experiencing morning fevers, abdominal pain with eating, nausea, non-bloody diarrhea, and decreased oral intake. During that time, she had two hospitalizations at an outside hospital for similar symptoms, where she was treated for pancytopenia and candidal esophagitis. On her last hospitalization, upper endoscopy showed duodenitis and colonoscopy showed ileitis with ulceration and colitis of the ileocecal valve. Abdominal CT showed wall thickening and inflammation involving the terminal ileum. On our examination, she was thin, with slow responses, oriented to person, place, but not time. Vital signs showed fever, tachycardia, and tachypnea. She had a diffusely tender abdomen with guarding in all quadrants. Rectal exam revealed brown, guaiac positive stool. Motor strength was 4/5 in all extremities. Physical examination was otherwise unremarkable. Chest radiograph and work-up for infectious and hematologic etiology were unremarkable. Serologic testing was positive for ASCA antibody, consistent with Crohn’s disease; however, Crohn’s diagnosis alone was not convincing and therefore, corticosteroid therapy was not started. The patient continued to deteriorate. Repeat abdominal and pelvic CT scans and colonoscopy confirmed findings of previous studies, except pelvic CT showed bilateral ovarian cystic and solid masses concerning for malignancy; therefore, prompting CT scan of chest which showed disseminated peripheral groundglass nodules and an indeterminate lung nodule. Quantiferon test was indeterminate. She was unable to produce sputum, requiring bronchial washings which revealed +1 acid fast bacilli.

Histopathology of the ileum showed multiple non-caseating granulomata and Mycobacteria tuberculosis. She was then started on quadruple anti-tuberculosis therapy, after which she became afebrile. On day 12 of therapy, she remained afebrile with improved appetite, energy and mobility. Follow up bronchial washings were negative and she was discharged home on a 9-month course of anti-tuberculosis therapy. This case illustrates the nonspecific presentation of disseminated tuberculosis, the stark similarity of tuberculosis ileitis with Crohn’s disease, and the importance of including intestinal tuberculosis in the initial differential diagnosis of chronic gastrointestinal symptoms, even in the absence of pulmonary symptoms.
CALIFORNIA POSTER FINALIST - CLINICAL VIGNETTE Grant Mayer

Acute Hepatitis and Pancreatitis Associated with Trimethoprim-Sulfamethoxazole

Grant Meyer BA, Kevin Chen M.D., Stephanie K. Zia M.D., FAAP, FACP

Introduction: Only a handful of cases have been reported in the literature discussing pancreatitis caused by trimethoprim-sulfamethoxazole (TMP-SMX). Even fewer cases of concurrent hepatitis have been described. We present a unique case of pancreatitis caused by TMP-SMX in an HIV patient that had yet to be started on highly active anti-retroviral therapy (HAART).

Case Description: A 37 year old Ethiopian male with history of HIV, diagnosed one week prior to admission, presented to the hospital with complaints of fever, headache, cough and abdominal pain. He was subsequently diagnosed with CNS toxoplasmosis, salmonella bacteremia, and suspected pneumocystis pneumonia (PCP), all susceptible to TMP-SMX. The patient improved clinically on TMP-SMX therapy and was discharged home with high dose TMP-SMX, dosed every 8 hours, Azithromycin for Mycobacterium Avium Complex (MAC) prophylaxis, and an HIV clinic appointment to initiate anti-retroviral therapy (ART).

The patient did well until fifteen days after initiation of TMP-SMX, when he began experiencing mid-epigastric pain associated with nausea and vomiting, anorexia, and extreme fatigue. He endured these symptoms for seven days until his scheduled follow-up visit in the HIV clinic, at which time he was admitted for further evaluation and management. Subsequent laboratory studies were consistent with acute hepatitis and pancreatitis. Bactrim was discontinued and the patient experienced rapid clinical improvement as well as downtrending laboratory values. The patient was switched to atovaquone for PCP treatment, pyrimethamine/leukovorin for toxoplasmosis, and ciprofloxacin to complete 4 weeks of salmonella bacteremia treatment. The patient was subsequently discharged when his symptoms resolved and laboratory findings improved.

Discussion: Hepatotoxicity caused by TMP-SMX is well documented and resolves with discontinuation of the drug, but there have been only eleven documented cases of TMP-SMX induced pancreatitis in the literature. Out of those eleven cases, four were associated with liver abnormalities and three occurred in HIV positive patients. For individuals with HIV, some ART medications used in HIV therapy are also known to cause elevated pancreatic enzymes, but our patient’s clinical course demonstrates how TMP-SMX pancreatitis can occur even in the absence of ART therapy. His pancreatitis developed after initiation of TMP-SMX and resolved immediately after discontinuation, which is highly suggestive of its causative relationship. Seven months after the discontinuation of the medication, the patient has no additional signs of hepatitis nor pancreatitis. This case highlights the importance in obtaining a thorough medication history and demonstrates the need to consider adverse effects of TMP-SMX in all patients who present with epigastric pain in the absence of other causes.
CONNETICUT POSTER FINALIST - CLINICAL VIGNETTE Allen Shih

Bacillus Cereus Bacteremia and MALDI-TOF

Allen F. Shih Matt Grant M.D. Christopher Sankey M.D., F.A.C.P.

A 65-year-old female presented to the emergency department confused, lethargic, and febrile after being arrested for cocaine possession. She had a history of HIV (CD4+ T cells 268 cells/mm3, VL undetectable sixteen months before admission), prior opioid dependence on methadone, and ongoing intravenous cocaine abuse. Initial physical examination revealed a cachectic female with a temperature of 104°F. Multiple needle track marks on the upper and lower extremities were consistent with active injection drug use. A systolic heart murmur was appreciated, but there were no cutaneous stigmata of infective endocarditis. Initial laboratory testing revealed a leukocytosis (14,500/ul) with neutrophilia (91%), and urine toxicology confirmed the presence of cocaine and methadone. Intravenous vancomycin was started empirically.

Blood cultures obtained for three consecutive days after admission were positive for a non-anthrax Bacillus species. Matrix-assisted laser desorption time of flight (MALDI-TOF) mass spectrometry was used to identify the bacteria as Bacillus cereus and to confirm all positive cultures grew the same species. A transthoracic echocardiogram (TTE) was negative for frank vegetation. Blood cultures were sterilized on the 6th hospital day and remained negative until discharge. She was given a total of 4 weeks of intravenous vancomycin at a skilled nursing facility.

Bacillus cereus is an aerobic, spore-forming, gram positive bacillus found in decaying organic matter, water, and human intestinal flora. It is typically associated with self-limited food-borne illnesses arising from ingestion of spores and from spores that contaminate fried rice and germinate when rewarmed. B. cereus also leads to more severe infections and bacteremia, and is a rare cause of endocarditis associated with IVDA, rheumatic heart disease, prosthetic heart valves, pacemakers, and immunodeficiency.

MALDI-TOF is a new, cost-effective technique in the rapid identification of bacteria. It requires preparing the bacterial sample, creating a spectrum fingerprint using mass spectrometry, and comparing the spectrum to others of known bacteria from a database. MALDI-TOF can identify bacteria under one hour with high specificity by profiling vast numbers of intracellular proteins. Bacterial drug susceptibility has also been obtained from MALDI-TOF, such as ampicillin-resistant E. coli and methicillin-resistant Staphylococcus aureus. Despite being accepted in Europe, MALDI-TOF systems have recently been approved in the United States. MALDI-TOF may soon become first-line in the identification of bacterial species.

This case illustrates the potential of MALDI-TOF to assist diagnosis and inform treatment of an acute bacterial infection. B. cereus bacteremia and endovascular infection are rare, and this technology allowed for rapid identification and confirmation of appropriate antimicrobial therapy.
Recognizing Anti-Synthetase Syndrome

David Maniscalco, Fourth-year medical student at Sidney Kimmel Medical College at Thomas Jefferson University David Michel, MD, Rheumatology at Christiana Care Health System

Introduction: Myositis, interstitial lung disease (ILD), “mechanic’s hands,” Raynaud’s phenomenon, fever and polyarthritis are clinical findings that characterize anti-synthetase syndrome. In this case, a 59 year-old African-American male presented with signs and symptoms consistent with polymyositis with a clinical picture of anti-synthetase syndrome. This case is unique because anti-synthetase syndrome is such a rare condition. Inflammatory myopathies occur in 0.5-8.4 cases per million. Of those cases, 30% of them result in anti-synthetase syndrome.

Case Description: A 59 year-old African-American male with a history of chronic polyarthritis presented to the hospital with hypotension and severe hypoxia. Over the preceding few months, the patient had experienced recurrent pulmonary symptoms thought to be due to pneumonia, for which he had been treated with antibiotics. His shortness of breath continued to worsen, however, and within 2-3 weeks preceding his presentation, he developed associated dizziness. Over the course of 2-3 months he noticed scaling of his first 3 digits bilaterally. He also reported difficulty with getting up from a seated position. On the day of admission, the patient spiked a fever of 39°C. Physical examination was remarkable for synovitis in his MCP joints bilaterally and severely restricted range of motion in his shoulders and elbows. The strength exam for hip flexion was 4+ out of 5 bilaterally. The palmar aspect of fingers 1-3 demonstrated severe scaling bilaterally. Laboratory findings demonstrated an elevated creatine kinase, an elevated lactate dehydrogenase, and a transaminitis. A chest CT scan from 2 weeks prior to admission demonstrated ground glass opacities and fibrosis consistent with ILD. An anti-extractable nuclear antigen was positive for anti-Jo1. Rheumatoid factor and anti-CCP were also positive. X-rays of his hands did not show erosions. An MRI of his thighs bilaterally, demonstrated active myositis. The patient was given a diagnosis of Jo-1 positive polymyositis with ILD with a clinical picture of anti-synthetase syndrome. The patient was started on Solu-Medrol and his symptoms improved. Azathioprine was suggested for long-term therapy.

Discussion: Even though anti-synthetase syndrome is a rare condition, this case highlights the importance of recognizing the characteristics of the syndrome early to reduce morbidity and mortality. The pieces of evidence from the history, physical exam, laboratory data, and imaging had to be compiled and evaluated to make the diagnosis in this case. Significant clues that may have been overlooked were his progressive dyspnea, which had been refractory to antibiotics, in conjunction with his musculoskeletal symptoms. A differential diagnosis of rheumatologic diseases that cause ILD should be thought of and should prompt a work-up that will lead to the correct diagnosis.
DISTRICT OF COLUMBIA POSTER FINALIST - CLINICAL VIGNETTE Jason Goldberg

A CALCIUM LEVEL OF WHAT?!

First Author: Jason Goldberg Second Author: Jonathan Cohen MD Third Author: Ruby Risal

A 52 year old previously healthy male presented to the emergency room with one week of nausea, vomiting, and abdominal pain. Aside from being a 1 PPD smoker and enjoying a six-pack of beer every day, he denied any significant medical or family history. His exam was notable for a sickly, dehydrated appearance, abdominal tenderness and an unsteady gait. Lab abnormalities included a lipase of 1957, creatinine of 2.8 and, most notably, a calcium level of 23.

Rechecked out of disbelief, it remained elevated at 21. The temptation to check again was resisted and IV Pamidronate, IV Calcitonin, and aggressive IV hydration was started in a monitored setting. Computed tomography of the abdomen and pelvis without contrast (elevated creatinine) showed pancreatitis, and four hepatic lesions, the largest measuring 6.6 x 5.3 cm.

After treatment was initiated, his calcium gradually trended down, his constitutional symptoms improved, and he was able to tolerate a diet. By hospital day 6, his calcium was 11.6 with a creatinine of 2. He was discharged home with a pending serum intact PTH and parathyroid related protein level (PTHrP) to complete his evaluation. The PTHrP returned elevated at 554 nl(14-27). This result made malignancy likely enough to biopsy a hepatic lesion without need for additional imaging studies. Pathology confirmed the presence of a metastatic, well-differentiated neuroendocrine carcinoma that was both synaptophysin and chromogranin reactive and suspected to be from a primary pancreatic lesion. Hypercalcemia occurs in up to 20% of malignancies, with squamous cell lung cancer being the most common, however, the patient’s slow response to treatment and dramatically elevated calcium and PTHrP levels led us to have a high suspicion for a secretory tumor rather than a primary lung malignancy.

Pancreatic neuroendocrine tumors (pNET) are rare secretory tumors generally associated with inherited syndromes, including neurofibromatosis and Multiple Endocrine Neoplasia type 1. There are ten specific pNET syndromes, with pNET causing hypercalcemia aptly termed PTHrPomas. With a primary location in the pancreas 100% of the time, the incidence of this syndrome is less than 0.1%/100,000/year. These patients generally present with both symptoms of hypercalcemia and hepatic lesions on imaging, illustrating that once the pNET metastasizes to the liver, the PTHrP can easily disperse throughout the body to cause hypercalcemia.

Though exceedingly rare, one must include PTHrPoma in a differential when confronted with an unusually high calcium level. The first step in the management of severe hypercalcemia is infusion of isotonic saline until a normovolemic state is reached. Adjunct IM or subcutaneous calcitonin may be administered concurrently for the purposes of rapid correction while IV bisphosphonate therapy is the mainstay of sustained treatment and correction.
Intussusception in a Patient with a History of Roux-en-Y Gastric Bypass

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**Introduction:** In adults, intussusception accounts for 1 – 5% of mechanical bowel obstruction. While rare, it should be included in the differential diagnoses of patients presenting with abdominal pain or symptoms of complete or partial bowel obstruction. Diagnosis is confirmed by CT scan and the treatment is surgical resection. Here we present a case of jejunal intussusception eleven years after a Roux-en-Y gastric bypass (RYGB).

**Case description:** A 55 year old Caucasian male with a medical history significant for morbid obesity, diverticulosis, irritable bowel syndrome, chronic pain, and anxiety presented with complaints of epigastric abdominal pain of 1 year duration described as intermittent and sharp and rated 10/10. The pain had worsened in intensity over the last three months. The patient’s appetite was decreased, and he had unintentionally lost forty pounds. He reported daily nausea and vomiting, but denied melena, hematochezia, or hematemesis. The patient’s surgical history was significant for RYGB in 2003, ventral hernia repair with mesh, esophageal dilation, and cholecystectomy. Physical examination was remarkable for hypoactive bowel sounds, abdomen was soft with neither guarding nor distension. He was afebrile with stable vital signs and no leukocytosis. CT of the abdomen and pelvis with oral contrast showed evidence of jejunal intussusception without signs of bowel obstruction. A small bowel follow through (SBFT) was performed which did not indicate a small bowel obstruction or telescoping bowel. However, a repeat CT again showed evidence of intussusception. Due to repeat CT evidence and history of recurrent abdominal pain likely secondary to intermittent intussusception, the patient was taken to the operating room for exploratory laparotomy. Active intussusception of the biliary limb was visualized proximal to the J-J anastomosis. The distal portion of the biliary limb was resected and the anastomosis was approximated 6 cm distal to the ligament of Treitz and 4 cm proximal to the J-J anastomosis. As early as post-operative day 1, the patient’s pain improved and was no longer occurring in “waves.” The patient’s nausea and vomiting ceased following surgery, and he was discharged on post-operative day five after full return of bowel function.

**Discussion:** This case illustrates a rare complication of recurrent small bowel intussusception in a RYGB patient that did not resolve with conservative therapy and required surgical resection. Clinicians should not be misled by a negative SBFT study. The combination of CT evidence of intussusception and patient presentation mandates surgery to resect the telescoping bowel.
Buried Balloon: a novel complication from percutaneous radiologic gastrostomy tube placement

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The need of gastrostomy tubes is expected to rise with our growing elderly population with more than 200,000 gastrostomy tubes being placed every year. Gastrostomy tube placement, once a staple of surgeons and gastroenterologists, has propagated into other fields of medicine. Interventional Radiology (IR) have started to perform Percutaneous Radiologic Gastrostomy (PRG) placement. With the increased role of IR in gastrostomy tube placement, there have been previously undescribed novel complications associated with this technique that have not been explored in the literature.

In the following case series, we describe three case studies that portray one of these specific complications as a result of PRG tube placement by IR, called the “Buried Balloon”. An analogous complication is the Buried Bumper syndrome (BBS) which has been extensively described in gastroenterology literature. Currently, there is a paucity of data in literature about the complications associated with PRG techniques specifically addressing this complication.
FLORIDA POSTER FINALIST - CLINICAL VIGNETTE Sean Verma

Something on My Mind: A Rare Case of Worsening Neurological Symptoms and Rapid White Matter Demyelination

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Acute Disseminating Encephalomyelitis (ADEM), an uncommon and incompletely understood autoimmune disorder of exclusion, is more frequently encountered in the pediatric population. This challenging diagnosis requires an extensive workup for more common entities.

A 53 year old gentleman presented to the emergency department with acute left arm weakness and altered mental status manifesting as difficulty with memory and performing activities of daily living. His past medical history was significant for neurosyphilis (treated with two weeks of IV penicillin G at an outside hospital 7 months prior to presentation) chronic hepatitis C, hepatitis B, bipolar disorder, and intravenous drug use. On exam he was alert and oriented to person, place, and time. Neurologic exam was significant only for 3/5 strength in the proximal and distal left upper extremity but otherwise intact to include reflexes, gait, and sensory testing. CBC revealed a leukocytosis of 16.88 x 10^9/L with a left shift and eosinophilia of 2.94 x 10^9/L. Initial laboratory work included an RPR which showed patient was in serofast state with a 1:8 titer (a significant reduction from previous) and HIV antigen/antibody test which was negative.

Following hospital admission, his symptoms continued to worsen. An MRI of the brain showed an extensive process involving the white matter bilaterally in both cerebral hemispheres with patchy areas of nodular enhancement without cavitation or ring like enhancing lesions. An extensive evaluation for cerebral demyelination was negative. This included: anti nuclear antibody, anti-nuclear cytoplasmic antibody, helminthic antibody testing, and paraneoplastic antibody testing.

A total of three lumbar punctures were performed over the following 8 weeks. The initial study demonstrated an elevated protein, normal glucose, and pleocytosis. Bacterial cultures, fungal stains, AFB, west nile, VDRL, HSV, EBV, CMV, JC virus, cryptococcal antigen, cytology, and flow cytometry were all negative. Oligoclonal bands were not present. A follow up MRI 10 days after the initial image showed progression of white matter changes. After extensive multidisciplinary consultation, literature search, and consideration, a diagnosis of ADEM was made and the patient was started on high-dose methylprednisolone and eventually underwent multiple treatments of plasmapheresis with radiographic improvement but incomplete clinical response. Ultimately, the patient was discharged to a nursing facility where he has demonstrated some recovery.

This case illustrates the challenge of diagnosing ADEM. Although frequently noted following a preceding illness or vaccination, ADEM can occur without inciting event, as in this case. The acute onset of neurologic symptoms which rapidly deteriorate over days in the setting of CNS white matter demyelination should raise suspicion for ADEM. Rapid detection and initiating aggressive early treatment may significantly improve prognosis of this disease however complete recovery is noted in a minority of the afflicted.
Cranial Nerve Palsy in the Setting of HIV / AIDS: Diagnosis and Treatment

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Introduction: Neurological and intracranial pathology in HIV+ patients has a broad differential diagnosis; optimal management of these patients requires a thorough understanding of infectious etiologies and diagnostic evaluations. Neurosyphilis may present with more rapid and devastating progression than seen in immunocompetent patients. ??

Case Description/History: 26 y.o. black male with h/o HIV (last CD4 reported 62, viral load 113k) off Atripla for 8 months presenting with acute onset diplopia, left sided tingling sparing the face, and difficulty with fine motor skills. Patient was in usual state of health until 1 month ago when he awoke with double vision. Since that time, symptoms had not progressed. Denied changes in visual acuity or other visual symptoms. One day prior to admission, patient awoke with tingling on the entire left side of his body sparing the face. No associated weakness, but difficulty with fine motor coordination in hands. Patient was afebrile with normal vital signs. Physical exam was notable for subcentimeter bilateral cervical LAD and inability to abduct right eye past midline. History of treated gonorrhea/chlamydia and syphilis.

Pertinent investigations:

- HIV: CD4 43, Viral Load 2380 K/mL.
- Lumbar Puncture: Glucose 39, Protein 223, RBC 2, WBC 52 with lymphocytic predominance.
- Microbiology Studies: CMV-PCR negative, EBV-PCR positive, HSV-PCR negative, JCV-PCR negative. Cryptococcal Antigen negative. Toxoplasma IgM negative. FTA positive, RPR positive 1:256, VRDL positive 1:32. ??

MRI/MRA: Numerous enhancing extra-axial foci on MRI brain images corresponding to aneurysms on MRA; these findings are most consistent with mycotic aneurysms. Patchy areas of increased T2/FLAIR signal in the cerebral white matter are nonspecific and may be related to HIV encephalopathy given the additional mild diffuse cerebral volume loss. ??

Hospital course: MRI/MRA of the brain was consistent with neurosyphilis with mycotic aneurysms and R brainstem CVA. Patient completed 14 day course of Penicillin G IV 24 million units per day. Initiated Truvada 1 tab, Darunavir 800mg, Ritonavir 100mg, and statin as inpatient. Patient was discharged home on hospital day 15 with persistent CN VI palsy.
**Discussion:** Immunocompromised patients have unique challenges for intracranial pathology and diagnostics. Neurosyphilis is a particularly destructive CNS pathogen due to its propensity to form mycotic aneurysms and significant risk of CVA. Syphilis is associated with decrease in CD4 count and increase in viral load, even in patients receiving antiretroviral therapy, which can be reversed with penicillin treatment. CNS invasion occurs in up to one-quarter to one-third of patients with syphilis, regardless of HIV status. Over half of neurosyphilis patients show no other signs or symptoms of syphilis; one-third of neurosyphilis cases in HIV+ patients are asymptomatic. AIDS (CD4 <200) is associated with decreased neurosyphilis response to penicillin treatment. After treatment, 30% of HIV+ patients have persistent symptoms at 6-month followup, and 5% show neurosyphilis relapse requiring retreatment.
GEORGIA POSTER FINALIST - CLINICAL VIGNETTE Jeffrey Tran

An Uncommon Presentation of Dizziness: The Story of GAD.

First Author: Jeffrey Tran Second Author: Alexander Reitz Third Author: Tiffany Morgan, MD Fourth Author: Noble Maleque, MD

Case Presentation: A 61 year-old female with insulin-dependent type 1 diabetes and hypothyroidism was admitted for a one-month history of worsening diplopia and nausea. Three months prior to her admission, she had experienced a sudden onset of persistent and debilitating ataxia, dysarthria, and dizziness. A saccadic defect consistent with pontine dysfunction on a rotary chair exam was identified and the patient was admitted for suspected paraneoplastic cerebellar syndrome. The testing for malignancy included a MRI of the head as well as a CT of the abdomen, chest and pelvis, all of which showed no evidence of malignancy. A paraneoplastic antibody panel including glutamic acid decarboxylase (GAD) antibody were sent during this admission. She was discharged with the results of the paraneoplastic panel pending. Upon this admission, her records were reviewed demonstrating an elevated GAD antibody of >250 IU/mL and anti-GAD65 of 411 nmol/L. For her diplopia, a MRI of her orbits was normal. At this point, an idiopathic autoimmune etiology of her gait ataxia, dysarthria, and diplopia was favored and a course of five days of IV methylprednisone was initiated. A lumbar puncture was also performed and her CSF was consistent with the preliminary diagnosis with an elevated GAD65 antibody. With administration of immunotherapy, she experienced moderate improvement of her dysarthria and was able to begin ambulating with the assistance of a walker. She was discharged to continue a course of oral prednisone. At her most recent follow-up appointment, two weeks after discharge, her nausea and dizziness had resolved but she continued to have intermittent diplopia and cerebellar ataxia.

Discussion: Glutamic acid decarboxylase is responsible for the conversion of glutamic acid into gamma aminobutyric acid (GABA), the major inhibitory transmitter of the CNS. Low levels of GAD65 antibody are commonly found in Type 1 diabetics. The onset of neurologic symptoms such as muscle spasms, muscle rigidity or gait ataxia accompanied by higher levels of GAD65 antibody are associated with a spectrum of neurologic disorders. Importantly, levels of GAD antibodies do not correlate with disease severity or response to therapies.

Conclusion: Patients with a history of autoimmune disease and new onset of a neurologic sequelae require prompt exploration of a possible autoimmune etiology and treatment with immunotherapy. Suspicion for GAD65 antibodies should be held for females with a history of Type 1 diabetes, particularly if patients present with cerebellar ataxia and additional symptoms of brainstem dysfunction such as dysarthria and ophthalmoplegia. While an underlying paraneoplastic process is rare in these patients with prior autoimmune disease, a thorough workup for a source of a potential neoplastic process should be pursued.
Beyond the hemolysis: Unexpected diagnosis of upper GI bleed in a sickle cell patient with coexisting gout and rheumatoid arthritis

Lillian L Tsai, Anand C Baxi, Cameron T Lambert MD, Lucas Golub MD, Lindsay Hannan MD, Joyce P Doyle MD

Case: A 51 year old African American male with a history of hemoglobin SS disease, high output heart failure, avascular necrosis, rheumatoid arthritis, gout, and upper GI bleed secondary to gastric ulcers presented with severe back, pelvic, and chest pain resembling past vaso-occlusive crises. The pain began when he fell and struck his right knee. He endorsed dizziness, nausea, and one episode of melena. He denied fevers, chills, cough, and abdominal pain. Home medications included NSAIDs and prednisone 10 mg daily. Pertinent exam findings included pulse of 121, moon facies, and conjunctival pallor. He had a moderate right knee effusion, swollen MCP andPIP joints bilaterally, and nodules on elbows bilaterally.

Labs showed WBC 26.6 K/mcl, hemoglobin 3.3 g/dL, hematocrit 11%, MCV 92 fL, RDW 28%, reticulocyte count 14.6% with an index of 1.5%, LDH 186 U/L, total bilirubin 1 mg/dL, and direct bilirubin 0.2 mg/dL. Peripheral blood smear showed few sickled cells and Howell Jolly bodies. In spite of packed RBC transfusion, his hemoglobin remained unstable. Without evidence of acute hemolysis but evidence of hypoproliferative anemia, major considerations included iron deficiency from blood loss, folate or B12 deficiency, or parvovirus infection. Further investigation revealed iron saturation of 13%. EGD found two large gastric ulcers. The etiology of his joint pain was investigated further as it was inconsistent with sickle crisis and causing significant distress. Labs showed uric acid 9.8 mg/dL and anti-CCP 88 units/mL. Arthrocentesis revealed negatively birefringent gout crystals. X-rays of hands and wrists were consistent with rheumatoid arthritis. The patient continued to have active bleeding and underwent antrectomy and truncal vagotomy. A 4 cm ulcer was noted to have eroded into the liver. Surgery was complicated by common bile duct injury and he expired from multisystem organ failure.

Discussion: This case demonstrates an unexpected cause of severe anemia and highlights the various complications of sickle cell disease. Chronic NSAID and steroid use contributed to gastric ulcer formation and a hyperuricemic state led to gout. Sickle cell anemia complicated the diagnosis of upper GI bleed by implicating a broad differential for severe anemia including hemolysis, aplastic anemia, and folate or vitamin B12 deficiency. Therefore, this case emphasizes the importance of using clinical reasoning and laboratory data to systematically evaluate anemia. This patient also represents one of the rare cases of coexisting gout and rheumatoid arthritis. To date only 52 cases have been reported. Current theories suggest that these processes inhibit each other via several mechanisms. Urate crystals have antioxidant and antiphagocytic properties and can block T and B cell activation. Rheumatoid arthritis produces IL-6 which has uricosuric properties. Thus, although it is possible for these diseases to coexist, it is unlikely for them to exhibit concurrent exacerbation.
ILLINOIS POSTER FINALIST - CLINICAL VIGNETTE Cindy Yen-chin Chen

Expect the Un-expected: Marked Urinary and Erectile Dysfunction with Short-Term Tramadol Use: Case Report

Cindy Chen Abdalla Hassan, MD

Introduction: Low back pain is a very common patient complaint, affecting as many as 84% of adults in their lifetimes. Treatment strategies include various pharmacologic and non-pharmacologic interventions; acetaminophen or nonsteroidal anti-inflammatory drugs are considered first line, but time-limited courses of opioids may be considered for debilitating pain that is not controlled with acetaminophen or NSAIDs. Tramadol is one such analgesic, the side effects of which most commonly include gastrointestinal disturbances, dizziness, and somnolence. In this report we describe a very unusual case of marked urinary symptoms and erectile dysfunction in association with a short-term use of tramadol.

Case presentation: A 29-year old man with no significant past medical history presented in our outpatient clinic with worsening lower back pain and sciatica. After multiple follow-up visits within four weeks and poor control of his pain on ibuprofen and gabapentin, tramadol was added to his pain regimen. After three days of starting tramadol, the patient reported total resolution of his lower back pain, but after the second dose of tramadol, he was experiencing increased urinary frequency. He recalled needing to urinate at least 15 times in a 24 hour period, including 9 or 10 times at night. He also noted erectile dysfunction, with absence of morning erections, inability to maintain an erection, and inability to ejaculate or obtain orgasm. He denied dysuria or any systemic symptoms. Tramadol was stopped and he was prescribed Norco instead. Interestingly, on follow up two weeks later, he reported complete resolution of his polyuria and erectile dysfunction within 24 hours of stopping tramadol in addition to satisfactory control of his pain.

Discussion: Polyuria and erectile dysfunction are very uncommon side effects of tramadol, reported in less than 1% of people taking the drug. The effects of tramadol on sexual function have led to its use in various studies for the treatment of premature ejaculation. Urinary dysfunction, though it has been reported, is even less common than erectile dysfunction. Those reporting these side effects have tended to be on tramadol for very long periods of time (two years or more), and have also tended to be older than age 50 years. The large majority had no resolution of symptoms with discontinuation of the medication. This case was very unique and interesting for its presentation with the combination of polyuria and erectile dysfunction in a relatively young healthy male. Moreover, we believe that this is the first case report to demonstrate such a rapid and aggressive onset of this combination of rare side effects as well as the complete resolution of the symptoms within 24 hours of Tramadol discontinuation.
ILLINOIS POSTER FINALIST - CLINICAL VIGNETTE Brian Lee

Chapter Winning Abstract

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Introduction: Crusted scabies is an uncommon form of scabies that is highly contagious and spreads by direct contact with an infected person. It tends to be associated with immune-compromised or elderly patients. Here we describe a case of an elderly immunosuppressed male patient who presented after a fall with septic shock. His crusted scabies was initially misdiagnosed as chronic exfoliative dermatitis. He had methicillin resistant Staphylococcus aureus (MRSA) and extended spectrum beta-lactamase (ESBL) Enterobacter cloacae septicemia. Review of the literature revealed that this is the first case of concomitant ESBL E. cloacae bacteremia in a patient with crusted scabies.

Case presentation: A 61-year-old Caucasian male nursing home patient on chronic immunosuppression for transplants presented after a fall and was found to be septic. He was initially treated for septic shock, and blood cultures revealed MRSA and ESBL E. cloacae complex. Despite no apparent source of infection, his extensive chronic dermatitis was the suspected source of the bacteremia. His skin cultures were positive for MRSA. Although the patient was in contact isolation, the diagnosis of crusted scabies was delayed until healthcare workers, who were in direct contact with the patient, presented with rashes. Laboratory tests confirmed scabies and he was started on scabetic treatment which slowly improved his rash. Infected individuals were treated, and close contacts were given prophylactic treatment.

Conclusions: Crusted scabies may initially resemble a chronic exfoliative dermatitis. Also bacterial super-infection of the rash and septicemia may be complications. This case highlights that a high degree of suspicion and prompt diagnosis can prevent the spread of crusted scabies in the healthcare setting. Due to the high infectivity of this form of scabies, this case highlights the need for both adherence to strict contact isolation and prophylactic treatment of exposed contacts.
ILLINOIS POSTER FINALIST - CLINICAL VIGNETTE Xavier Pereira

Pulmonary artery rupture: a potentially life-threatening complication of pulmonary artery hypertension, a case report.

First Author: Xavier Pereira, Karthik Ragunathan, Karthiek Narala, Sandeep Banga

An 80-year-old Caucasian female with a past medical history of hypertension, coronary artery disease, and idiopathic pulmonary artery hypertension (WHO Group I), presented to the hospital with severe substernal chest pain lasting one day. The chest pain radiated to her back and was associated with nausea, vomiting and diarrhea. The patient denied a history of recent trauma, dyspnea, fevers or chills. She had a 10-year history of severe pulmonary arterial hypertension (PAH) treated with bosentan, tadalafil and 3 liters of continuous oxygen. Other medications included aspirin, warfarin, diltiazem, and lisinopril-HCTZ. Physical examination was significant for blood pressure of 110/56, heart rate of 101, respiratory rate of 27, oxygen saturation of 90% on room air, a regular cardiac rhythm without murmurs, and mild bibasilar crackles on auscultation. Laboratory findings revealed a hemoglobin of 14 g/dL, PT of 16.5 sec, INR of 1.3 and PTT of 44 sec. On admission, her arterial blood gas showed a pH of 7.34, pCO2 of 43 mmHg, pO2 of 57 mmHg, and bicarbonate of 25 mEq/L. She underwent a ventilation-perfusion (V/Q) scan that suggested a high probability of pulmonary embolism. Electrocardiogram exhibited normal sinus rhythm with nonspecific T-wave changes. Trans-thoracic echocardiogram showed a dilated right atrium and right ventricle, right ventricular hypertrophy with an ejection fraction of 55-60%, and a mild pericardial effusion. Computerized tomography (CT) angiogram of the chest was negative for pulmonary embolism but revealed extravasation of blood into the pericardium from the inferior right pulmonary artery measuring 1.4 x 1.1 cm without evidence of dissection, a moderately sized pericardial effusion, and bilateral pleural effusions. These findings were the result of a spontaneous rupture of the inferior margin of the right main pulmonary artery. Due to her extensive comorbidities, the patient and her family opted for hospice care.

Pulmonary artery rupture (PAR) is a potentially life-threatening and rare complication of longstanding PAH. However, given the rarity of this disease, there is little information on the pathophysiology, precipitating factors and management of this condition. Historically, many types of invasive procedures have been attempted with varying degrees of success. Yet, in the absence of tamponade, hemodynamic instability or ongoing blood loss, surgical intervention may not be indicated in high-risk patients. This case highlights the importance of considering PAR in the differential diagnosis of PAH patients presenting with severe chest pain. PAR should be considered within the spectrum of complications of PAH that classically includes arterial wall dilation, aneurysm, and dissection.
KANSAS POSTER FINALIST - CLINICAL VIGNETTE Joseph A Moore

Small lymphocytic lymphoma presenting with hypopituitarism

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INTRODUCTION: Non-Hodgkin lymphoma represents 4.3% of all new malignancies in the United States annually. Small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL) presents primarily with lymphadenopathy, constitutional symptoms and/or abnormal CBC. Central nervous system (CNS) involvement with SLL/CLL is rare. We describe a patient with SLL/CLL presenting with hypopituitarism due to sellar involvement.

CASE DESCRIPTION: A 71-year-old Caucasian male presented with fatigue, cold intolerance and decreased alertness. The physical exam was unremarkable, including normal visual fields. Lab studies showed low TSH (0.407) with low free T4 (0.034 ng/dL), indicating secondary hypothyroidism. Additional studies showed low testosterone (< 3 ng/dL) and cortisol level (5.3 mcg/dL). MRI of the brain revealed a 1.1 x 1.8 x 1.1 cm enhancing suprasellar mass, abutting the optic chiasm without displacement. Transsphenoidal resection revealed SLL/CLL. Post-operative MRI revealed residual enhancing tissue (0.8 x 1.8 x 0.6 cm). CT of the neck, chest, abdomen and pelvis revealed bilateral axillary and hilar lymphadenopathy. PET-CT imaging showed subcarinal uptake (SUV 3.4). Bone marrow biopsy revealed stage IVA SLL/CLL. The patient received thyroid and corticosteroid replacement. Tertiary institution referral resulted in a recommendation for radiation to the pituitary, which was well tolerated with the exception of transient visual symptoms. The patient is monitored with serial MRIs, with systemic therapy reserved for disease progression.

DISCUSSION: Treatment of CNS lymphoma is challenging due to difficulties of medications crossing the blood-brain barrier, resulting in low cerebrospinal fluid concentrations. Therapeutic challenges in this patient included a low mitotic rate and low CD20 expression. Radiation therapy was considered for this patient due to the location and low-grade nature of the tumor. The therapeutic goal was to prevent local recurrence. Toxicity concerns included the close proximity of the optic chiasm with potential visual loss and the risk of permanent panhypopituitarism. The most sensitive hormone is growth hormone, with dysfunction seen after 20 Gy. Anterior pituitary hormones are more radiosensitive at doses of 30 Gy or higher. The posterior pituitary is the most radioresistant, with only rare episodes of diabetes insipidus observed. This patient was successfully treated with radiation therapy using a dose of 24 Gy, having achieved complete resolution of the pituitary tumor. He remains alive and asymptomatic. This case describes a patient with SLL/CLL manifesting as hypopituitarism. This patient represents only the fourth such case described. Consideration of therapeutic options proved to be complex, but a complete remission was achieved. Future reports may be of assistance to clinicians in therapeutic decision-making.
INTRODUCTION: Podoconiosis, is a non-infectious non-filarial type of Elephantiasis that is considered a neglected tropical disease (NTD). (Davey and Newport 2007) Although preventable, podoconiosis is a geochemical inflammatory response triggered by consistent barefoot exposure to red-clay soils in highland areas of Tanzania and other countries. Known as mossy foot for the moss-like papillomata, podoconiosis can have two contrasting presentations: a soft-fluid “water bag” type of edema or hard and fibrotic. (Davey, Tekola et al. 2007) We feature three cases of podoconiosis to illustrate the clinical diversity of this rare disease.

CASE PRESENTATION: All patients are HIV positive and live in the Mufindi region of Tanzania, a mountainous area with red-clay soils.

- Patient 1: A 33 year-old female whose chief complaint was foot irritation. She has a 3-year history of foot burning, irritation, and bilateral swelling of the feet, ankles and legs to the knee joint. Her toes were block-shaped and exhibited mossy-like papillomata.
- Patient 2: A 30 year-old female whose chief complaint was epigastric pain. She presented with bilateral edema most pronounced on the dorsum of the feet and progressing to the knee joints. Her toes were block-shaped and exhibited mossy-like papillomata.
- Patient 3: A 41-year old male whose chief complaint was pain from an infected ulcer on the lower left leg. He had an 8-year history of irritation and ascending lymphedema on his left leg stopping just below the knee and mossy-like papillomata up to his left ankle. His right foot exhibited moderate lymphedema.

DISCUSSION/CONCLUSION: As clinicians in the field it is important to distinguish between the two types of elephantiasis for diagnostic and treatment purposes. While lymphatic filariasis, is caused by a nematode infection and presents with a descending unilateral swelling of the lower limb or genitalia. Podoconiosis, has a bilateral ascending lymphedema that terminates at the knee. Although the extent and characteristic of the lymphedema can vary, the appearance mossy-like growths and block shape toes prove to be consistent characteristic of all podoconiosis patients. Being that podoconiosis is entirely preventable, its prevalence may be reduced if community health workers are educated about its etiology, presentation, preventative measures and treatment. Podoconiosis is often misdiagnosed and believed to be infectious, which prevents proper treatment. We aim to bring the etiology and diagnostic protocol of podoconiosis to the attention of providers in endemic regions.

Weighting for Love

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INTRODUCTION: Gelatinous Bone Marrow Transformation (GMT), also known as ‘Starvation Marrow’, is a rarely diagnosed disorder. GMT is characterized by a focal loss of hematopoietic cells, fat cell atrophy, and a deposition of extracellular gelatinous substances rich in hyaluronic acid. It is often seen in younger patients with anorexia nervosa, acute febrile states, or AIDS; in middle aged patients with alcoholism, or lymphomas; and in older patients with chronic heart failure.

CASE PRESENTATION: A 58-year-old white male presented to the E.R. complaining of a week long history of severe fatigue, nausea and darkened urine. His past medical history included hypertension, A.D.H.D., and depression. Examination revealed an ill appearing, febrile, slightly obese (180lbs) male, with scleral icterus. The remainder of exam was unremarkable. Laboratory results were significant for thrombocytopenia and trans-aminitis (see table). Imaging was unremarkable. Initial differential included sepsis, Disseminated Intravascular Coagulation, Thrombotic Thrombocytopenic Purpura, Evans Syndrome, and a primary marrow disorder.

A bone marrow biopsy revealed no obvious malignant transformation. Colloidal iron staining revealed areas of blue infiltrate (Fig. 1), which then greatly decreased after pre-treating with hyaluronidase (Fig. 2), consistent with deposition of hyaluronic acid. A diagnosis of Gelatinous Bone Marrow Transformation (GMT) was considered likely.

A more detailed social history revealed the initiation of a very fastidious vegan diet, coupled with an aggressive exercise regime 4 months prior to his presentation. He had lost more than 70 lbs in that time. His diet began after his online potential fiancé claimed that she would move to North America to marry him only if he ‘got into shape’. The patient began an enriched nutritional program and a short course of tapering prednisone. At the end of two weeks the liver enzymes, platelet counts and white cell indices had returned to normal.

DISCUSSION: GMT is seldom seen in adult males in the absence of severe alcoholism or chronic illness such as lymphoma. On initial assessment this patient did not show stigmata of anorexia or features of a chronic wasting disease, and was a non-drinker. He did not volunteer the dietary issues until later in his admission and this knowledge helped direct the subsequent evaluation and therapeutic approaches. Clinicians should remain aware that eating disorders and body dysmorphic disorder are not only a condition of females. The nutritional assessment remains an integral component of a comprehensive medical history.
Lung Herniation

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Lung herniation can be described as a protrusion of lung parenchyma along with its accompanying pleura beyond the bounds of normal thoracic cavity under the skin. This is a very rare and extraordinary phenomenon.

A 49-year-old male presented to clinic with worsening dyspnea, decreased concentration and fatigue. He has significant medical history of asthma, tobacco use, obesity, sleep apnea and sarcoidosis. An incidental discovery during physical examination revealed a swollen mass just below the right mid-clavicular line with an overlying scar. The mass was non-tender, round, soft with smooth border, and sized roughly 4 cm in diameter. The most prominent feature was that, upon deep inspiration and coughing, the mass ballooned out of the patient’s chest wall. Upon questioning at that time, the patient was not aware of the etiology of the bulge but reported a diagnostic biopsy procedure which took place nine years ago for suspected sarcoidosis. A two-views chest x-ray showed a 5.6 x 5.4 x 2.9 cm well-defined oval radiolucent area, suggestive of lipoma or other benign appearing lesions. Ten days after the initial visit, the patient went to emergency department for worsening dyspnea, increased chest pain and significant ballooning requiring manual reduction after coughing spells. A computed tomography of the chest was ordered, which revealed an atypical right second rib missing its medial end with herniation of lung parenchyma through the defect between the rib and the sternum. Further investigation into patient’s operative report for the mediastinotomy lymph node biopsy showed removal of the patient's second right intercostal cartilage for adequate access to the right hilum. Over the following weeks, the patient was becoming more symptomatic and the defect was eventually repaired with Gore-Tex soft tissue patch without any post-operative complications.

Herniation of lung parenchyma with its pleural membranes is a rare consequence of congenital or acquired defect in one’s thoracic chest wall. Most patients with lung hernia are asymptomatic or present with non-specific symptoms. This case serves to remind the health-care community to recognize lung hernia within the complications of thoracic surgery. No substantial data exists to postulate the true extent of respiratory impairment due to lung herniation. However, a few possible complications may include recurrent infection, pneumothorax and strangulation of entrapped lung tissue. Therefore it is important to educate physicians on such rarity, or so-called “zebra diagnosis,” in order to provide the best care for patients with history of thoracic surgery.
Severe hypercalcemia secondary to sarcoidosis of the bone - A case report

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Sarcoidosis is a multi-system granulomatous disorder with manifestations most commonly in the lungs. Skeletal involvement is rare, reported in 1-13% of sarcoidosis cases; hypercalcemia can be one of its presenting signs.

A 70-year-old woman presented to the emergency department with general malaise and fatigue. She has a history of diabetes mellitus type 2, hypertension and dyslipidemia for which she takes Metformin, Nifedipine and Simvastatin. She had normal vital signs, no mental status changes, and physical exam was unremarkable. She was found to have severe hypercalcemia to 15.9 mg/dL and acute kidney injury with Cr 2.15 mg/dL. Further investigation revealed PTH 13 pg/mL (normal 15-65 pg/mL), PTHrP <0.74 pmol/L (normal <2.0 pmol/L), ACE level 134 U/L (normal 14-82 U/L), 25OH-Vitamin D 27.8 ng/mL, and 1,25-Vitamin D 166.6 pg/mL. Mammography and colonoscopy were normal in the past year. Chest radiography and CT of the chest revealed several small right upper lobe pulmonary nodules and mediastinal and hilar lymphadenopathy suggestive of sarcoidosis. Skeletal survey revealed lucency in the right humerus without any cortical bone thickening or other signs of Paget's disease. SPEP analysis was negative and bone marrow aspirate and core biopsy revealed multiple small non-caseating granulomas. She was diagnosed with hypercalcemia secondary to bony involvement of sarcoidosis. She was treated with high dose prednisone, aggressive fluid hydration, and intramuscular calcitonin. The patient's calcium decreased to 11 mg/dL and her acute kidney injury resolved within 48 hours.

Sarcoidosis of the bone is usually found in patients with known pulmonary sarcoid and is rarely a presenting feature of the disease. Radiological findings show lace-like honeycomb cystic and lytic lesions of cortical bone, with cavities of varying sizes and surrounding sclerosis. Skeletal sarcoidosis usually affects the phalanges in the hands and feet, but has also been described in the nasal bones and vertebrae. Involvement of the humerus and long bones is extremely rare. The differential diagnosis includes metastasis, hyperparathyroidism with secondary brown tumors, Paget's disease, multiple myeloma and lymphoma. Skeletal sarcoidosis is rarely seen in the absence of skin lesions and 80-90% of cases have evidence of pulmonary involvement. To our knowledge, this report describes the first case of lytic humerus lesions and secondary hypercalcemia as the presenting sign of sarcoidosis.

Hypercalcemia can be a life-threatening emergency. Although skeletal sarcoidosis is a rare condition, physicians, especially, in the hospital setting should have a high index of suspicion for sarcoid-induced hypercalcemia. Treatment of hypercalcemia secondary to sarcoidosis consists of a low calcium diet, adequate hydration, and minimizing sunlight exposure and steroids to reduce overproduction of calcitriol in activated macrophages.
Sudden visual loss as the single manifestation of secondary syphilis

The incidence of syphilis has been rising worldwide over the last decade due to the increasing rate of high-risk sexual behavior. Syphilis can present with a wide array of clinical symptoms, making it difficult to diagnose. In the setting of ocular disease, uveitis appears to be the most common form of syphilitic eye involvement, while optic neuritis occurs infrequently.

We describe a case of a 52-year-old man with HIV infection who was hospitalized because sudden unilateral visual loss. Previous medical history revealed primary infection of syphilis, and gonorrhea at age of 20 years successfully treated. HIV infection was diagnosed in 2007 and the patient is currently under HAART based on tenofovir, emtricitabine and atazanavir/ritonavir. VDRL was negative 5 months earlier. Last T-CD4+ cell count was 591cell/mm³ and the HIV-RNA plasma viral load was 69 cop/ml

Clinical examination was remarkable for submandibular and cervical nontender lymphadenopathy. Intra-orally there was a 2-cm nontender painful ulcer in the floor of the mouth. Visual acuity in the left eye was 20/400. Examination showed no other abnormalities. The optical coherence tomography (OCT) was normal.

MRI showed left optic nerve hyperintensity in transverse and coronal gadolinium-enhanced fat-saturated T1-weighted images. Visual fields test by SITA-Standart strategy with white stimulus III revealed: Left eye: central scotoma, mean deviation (MD) of -11.43dB P<5% and a pattern standard deviation (CPSD) 12.18dB P<5% compatible with acute retrobulbar neuritis. Right eye: MD of -4.52 dB P< 5% and CPSD 4.45dB P<5%. Serum non-treponemal test (VDRL) was positive (1:128) and negative in cerebrospinal fluid (CSF). FTA test was positive in both fluids.

The patient was treated with daily 24,000,000 IU of intravenous penicillin G sodium in addition with 1mg/kg of prednisone for 14 days. After treatment visual acuity in the left eye was 20/70 and the visual fields test showed the following: Left eye: improvement of central scotoma with MD of -4.21dB P< 5% and a CPSD 4.26dB P<5% and right eye: MD of -1.81 dB P< 10% and CPSD 2.26dB P<5%, showing improved central vision in both eyes.

Ocular involvement can be the single manifestation of secondary syphilis and a high diagnostic suspicion is necessary, particularly in high-risk populations.
Building muscles at the cost of your kidneys: A unique case of creatine-induced IgA nephropathy

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Introduction: Bodybuilders commonly use non-FDA approved dietary supplements as a nutritional ergogenic aid. Creatine is the most popular of these substances, believed to enhance muscle mass and help athletes achieve bursts of strength. Daily maintenance dose of 2 to 5g of creatine was deemed safe by some studies. However, there have been limited case reports of creatine induced interstitial nephritis and postadaptive focal segmental glomerulosclerosis (FSGS). Herein, we present a unique case of IgA nephropathy due to excessive intake of creatine.

Case description: Patient is a healthy 29-year-old Caucasian male, known body builder, presenting with a one-day history of penile, scrotal and bilateral lower extremity swelling. Two days prior, he had generalized myalgias and dry mouth resulting to polydipsia. For the past five years, patient was using a supplement, which contained creatine monophosphate (5g), glutamine (5g) and multivitamins. On physical examination, patient had elevated blood pressure of 140/90 mmHg. He also had bilateral 2+ pitting edema in lower extremities and a nonerythematous, edematous penile shaft with bilateral scrotal swelling. Initial work up revealed hypoalbuminemia at 1.9 (2.8- 5.5 g/dl) and serum creatinine of 1.4 (0.5-1.5 mg/dl) along with proteinuria, microscopic hematuria and course granular hyaline casts on urinalysis. Renal ultrasound (US) and US duplex scrotal/testicle were unremarkable. Antinuclear antibody (ANA) and anti-neutrophil cytoplasmic Antibody (ANCA) were negative. Complement C4 level was normal and C3 was mildly decreased. A 24-hour urine protein showed nephrotic range proteinuria at 6322.5 (0-225mg/24hr) and protein/creatinine ratio of 3.5 (0-0.1). Patient was diagnosed to have nephrotic syndrome. Patient was started on methylprednisone, furosemide and intravenous fluids. Renal biopsy was performed which showed crescentic IgA nephropathy (IgAN) with minor components of FSGS and podocyte foot process effacement. On fifth-day of admission, the patient was discharged with moderate improvement of edema. He was instructed to restrict the fluid intake to 1.5L/24hrs, consume a low protein diet and discontinue all supplements. On two-week follow-up, the protein/creatinine ratio worsened to 7.1 from 3.5 suggesting a worsening proteinuria. The patient was then started on olmesartan and steroids were continued.

Discussion: Although creatine is a natural substance, it hasn't been well studied over the long-term side effects. In this case, patient’s renal disease (IgAN) is most likely from the prolonged intake of high doses of creatine. Rapidly progressive glomerulonephritis (RPGN) is rare sequelae of IgAN and nephrotic range proteinuria (urine protein >3.5gm/day) is only found in about 5% of the cases of IgAN. Furthermore, since 10% of IgAN cases are idiopathic, this case raises the question whether creatine is a rare cause of idiopathic IgAN. Therefore, consumers should balance the quality of information supporting the use of creatine with the possible risks of using the product, including possible renal dysfunction.
Apical Hypertrophic Cardiomyopathy: A “Giant-Negative” Diagnosis

Introduction: Apical Hypertrophic Cardiomyopathy (A-HCM), a variant in which the hypertrophied myocardium is located in the most distal portion of the Left Ventricle (LV), was first described in Japan in 1976. Prevalence of this variant represents only 1-3% in the non-Japanese population. Symptoms may include dyspnea and palpitations, reflecting the reported arrhythmias associated with this condition.

Case Report: A 61-year old African American gentleman with past medical history of intermittent atrial fibrillation, hypertension, and COPD presented to the emergency department (ED) in an extremely somnolent state with chief complaints of shortness of breath and a “pounding heart”. On physical exam he was malnourished, dehydrated, and tachycardic at 100 beats per minute with a 5/6 holosystolic murmur heard best at the left sternal boarder. PMI was visible and displaced infero-laterally. There was decreased air movement globally and a prolonged expiratory phase. Arterial Blood Gas drawn in the ED showed pH = 7.39, CO2= 76, HCO3 = 36 and O2 = 86 with no wheezing, likely reflecting compensated COPD; not an acute exacerbation. Chest radiograph showed emphysematous changes without pulmonary infiltrates. His clinical condition limited the history of present illness, leading to an EMR review exposing several ED visits. On admission 8-months prior, an ECG was performed showing apical left ventricular hypertrophy evidenced by R-waves ranging 2.0 to 3.0 mV and deeply inverted (“Giant-Negative”) T-waves (> 1.0mV) in leads V4-6. However, it was not until a later, separate, admission that a Transthoracic Echocardiogram (TTE) was ordered in response to an indeterminate troponin. TTE revealed a morphologic appearance consistent with apical variant hypertrophic cardiomyopathy including disproportionate apical segment hypertrophy, visually estimated ejection fraction >80% with impaired relaxation pattern, and near cavity obliteration at the apex in systole. The abnormal ECG and TTE findings were combined with our patient’s presentation and physical exam to, at last, establish a diagnosis of Apical-HCM. Normal saline at 100 ml/hr. and 2 L/hr. of oxygen via nasal cannula were started. Our patient became increasingly more alert and less dyspneic. He was counseled on the importance of adequate hydration, as his cardiovascular morphology is fluid dependent, and adherence to Metoprolol for increased ventricular filling time.

Discussion: Since our patient had not received an appropriate and conclusive diagnosis of A-HCM, it is likely his COPD (resulting in recurrent ED visits with only slight improvement) and its rare occurrence in the non-Japanese population actually masked the true underlying cause as A-HCM. Therefore, abnormal cardiovascular findings on physical exam, as evident in our patient, should strongly alter the workup to pursue an alternative diagnosis. Thus, recognition of the distinctive ECG and TTE findings are vital in diagnosing A-HCM; especially in patients presenting with dyspnea, palpitations, and displaced PMI.
Seizing the Opportunity to Avoid Premature Closure.

First Author: Maros Cunderlik, MS-3 Second Author: Andrew Olson, MD

Determining etiology of an apparent syncopal episode is essential to the subsequent treatment and prevention of future episodes. The diagnostic process is often complicated by the fact that several non-syncopal diseases can mimic syncope and most syncope is not associated with life threatening etiologies.

Case: A 49 year old man was found on the floor of an elevator one evening by his colleagues while working as a custodian. In the Emergency Department he reported waking up to people slapping him in the face. The episode was not directly observed and the last thing he recalled was walking into the elevator approximately 30 minutes earlier. His pants were wet in the ED but was unsure if he was incontinent. He had no complaints of tongue biting, chest pain or dyspnea and reported no prodromal symptoms. He did report two similar episodes in the past three months which were both unwitnessed. Past medical history was significant for a distant history of head injury as a teen and meningitis at nine months with subsequent right arm contracture. His physical exam was unremarkable with no cardiovascular or neurological abnormalities except his right arm weakness with contracture. Further workup including ECG, head CT, electrolytes and glucose showed no abnormalities. He was admitted to the hospital overnight for further evaluation. Next morning the patient was noted to be ‘out of it’ and had a brief episode of loss of consciousness. ECG showed sinus slowing without PR prolongation leading to a sinus arrest with 24 seconds of asystole. As a result an emergent permanent pacemaker placement was performed. However, the patient continued to have episodes of hypoxia, pacemaker dependent bradycardia and altered mental status after the pacemaker was placed. Given these findings a video EEG was performed that revealed interictal epileptiform discharges in the right frontotemporal area consistent with seizure activity. Consequently the patient was treated with levetiracetam and remains seizure and asystole free at six months following the initial hospitalization.

In conclusion, ictal asystole is a rare but potentially life threatening complication of epileptic seizures. As this case demonstrates, an episode of apparent syncope with evidence of sinus slowing or asystole warrants both detailed cardiac and neurologic assessments and evaluation should not "stop with the heart."
Fever of Unknown Origin: Sometimes a Zebra is a Zebra

First Author: Nikhil A Patel M.Sc. Second Author: Meltiday Issa M.D. FACP

**Introduction:** In adults, fever of unknown origin (FUO) is primarily infectious, neoplastic, or autoimmune in etiology. It is characterized by a prolonged febrile illness without an established etiology despite intensive evaluation and diagnostic testing. When the history, examination, or imaging uncovers a possible source, specific testing should be performed. Biopsy is a specific and critical modality in the directed evaluation of FUO especially when thrombocytopenia and anemia are present. Therapeutic trials of antimicrobials or glucocorticoids are tempting but rarely establish a diagnosis.

**Case Description:** A 69-year-old South Sudanese woman presented to outside hospital with fever and productive cough. She was diagnosed with sepsis secondary to streptococcus pneumonia by urine antigen. She responded to fluid resuscitation and was kept on levofloxacin to complete a 7 day course after dismissal from the hospital.

Two weeks later she presented again with similar symptomology along with anemia and thrombocytosis. This time she continued to deteriorate despite multiple IV antibiotics and required ICU level of care. Extensive infectious disease workup yielded only a positive QuantiFERON-TB test and a negative HIV antibody assays. CT of abdomen and pelvis revealed mesenteric lymphadenopathy and bilateral axillary lymph adenopathy. Right axillary lymph node aspiration was performed but was non-diagnostic. CT/PET scan again showed persistent mesenteric and axillary lymphadenopathy as well as a hypermetabolic spleen. Excisional biopsy pathology of right inguinal lymph node revealed HHV-8 positive, MCD. She was initiated on rituximab and ganciclovir therapy. For the history of latent TB infection, she was started on isoniazid with vitamin B6. She improved dramatically with this therapy and was discharged to follow up as an outpatient with hematology and infectious disease.

**Discussion:** Castleman’s disease in its multicentric form is strongly associated with immunosuppression, HIV, and HHV-8 infection. Despite many cases associated with HIV infection, non-HIV, HHV-8 positive MCD can also occur. Diagnosis should be suspected in patients with fever, splenomegaly, and peripheral lymphadenopathy. CT imaging should also illustrate multiple regions of involvement and one irregular node should be excised for biopsy. First line treatment for HHV-8 positive, MCD is rituximab (anti-CD 20 antibody) and ganciclovir. With only ten patients in the literature identified as HIV negative, HHV-8 positive MCD, seven have died, many within several months after diagnosis. This case highlights the importance of a team-based approach in evaluating complex FUO cases where the internist plays a key role not only as a great diagnostician but also as a leader and care coordinator.
Primary laryngeal actinomycosis masquerading as vocal cord leukoplakia in the absence of predisposing risk factors

First Author: Benjamin Goege Second Author: David Kowalczyk Senior Author: John Schweinfurth

Introduction: Primary actinomycosis of the vocal cord is an exceedingly rare disease that has been reported only a few times in the literature, usually in the presence of predisposing risk factors. Actinomycosis in humans is most commonly caused by the Gram-positive anaerobe Actinomyces israelii that is part of the normal oral flora and manifests as cervicofacial disease. Here we present a case of laryngeal actinomycosis in a patient presenting with dysphonia.

Case Report: A 50-year-old white female with a 34-pack-year smoking history and multiple recent bouts of atypical pneumonia presented for evaluation of dysphonia. She reported hoarseness for one year worsened by stress along with intermittent episodes of losing her voice completely. She also reported globus pharyngeus but denied dysphagia or any other complaints. She was diagnosed with acid reflux at an outside hospital and treated with anti-reflux medications to no avail. On exam the patient expressed mild vocal dysphonia. No adenopathy, thyroid enlargement, or lesions on the inside of the mouth were noted. Laryngoscopy revealed a lesion on the right true vocal cord with asymmetric mobility but complete glottis closure. Additional nasopharyngeal and physical exam findings were otherwise unremarkable. Patient was taken to operating room for biopsy of lesion suspicious for vocal cord leukoplakia. A sessile whitish lesion was excised from the superior surface of the middle third of the right true vocal cord. The patient was placed on voice rest two weeks following the procedure. Histopathology revealed an acute fibrinopurulent inflammatory lesion positive for Actinomyces, but no evidence of neoplasia or virocytes. The patient was started on amoxicillin 500 mg orally three times per day for two months with scheduled follow-up to monitor continued resolution of actinomycosis.

Discussion: The incidence of actinomycosis in humans is relatively uncommon with most major medical centers diagnosing around one case per year. Predisposing factors include dental disease, diabetes mellitus, and immunosuppression. The infection classically presents as a slowly progressive mass that develops into multiple abscesses of soft tissue that can occasionally progress to bony invasion. The most frequent sites of infection include the cervicofacial region, lung, abdomen, and genitourinary system in women with intrauterine devices. Primary presentation in the vocal cords is extremely unusual, especially in the absence of orofacial trauma or predisposing risk factors. Laryngeal dysplasia and carcinoma are frequent causes of vocal cord lesions and concurrent dysphonia. Patients, especially those with a history of smoking, found to have vocal cord lesions require biopsy to rule out leukoplakia or cancerous lesions. Although uncommon, this case report demonstrates the need for consideration of actinomycosis in the differential diagnosis for vocal cord lesions, even in the absence of predisposing risk factors.
MISSOURI POSTER FINALIST - CLINICAL VIGNETTE Nila Manandhar

A Rare Case of Tension Pneumocephalus in a Patient Diagnosed with Nasopharyngeal Squamous Cell Carcinoma (NPC)

Nila Manandhar, M4 Shahzad Raza, M.D., Post-doctoral fellow/Hematology/Oncology Rashmi Ramasubbaiah M.D., M.S., Post-doctoral fellow/Hematology/Oncology Donald C. Doll, M.D., Professor of Emeritus/Hematolgy/Oncology

Introduction: Tension pneumocephalus occurs when air is trapped within the cranial cavity. It is associated with neurosurgical procedures, trauma, and meningitis. Here, we report a rare case of tension pneumocephalus in a patient diagnosed with NPC after concurrent chemoradiation.

Case Presentation: The patient is a 56-year-old Caucasian male diagnosed with locally advanced NPC (T3 N0 M0). He was treated with concurrent chemoradiation with intensity-modulated-radiation therapy at a dose of 7000 cGy in 35 fractions for seven weeks and cisplatin 100mg/m² (days 1, 22, and 43). This was followed by two cycles of cisplatin 80mg/m2 (day 1) and fluorouracil (5-FU) 1000mg/m2 (days 1-4).

After completion of chemotherapy, the patient presented with fever, intractable headaches, and intermittent cerebrospinal fluid (CSF) rhinorrhea. Head CT showed erosion of the clivus with associated CSF leak along with scattered air pockets in the subarachnoid spaces and ventricular system, indicating pneumocephalus. CT-Neuronavigational Sinus Study identified contrast leakage from the roof of ethmoidal air cells. Even though patient underwent endoscopic repair of the leak, closure of the CSF fistula, and placement of ventriculo-peritoneal shunt, his clinical course was complicated by multiple infections, free flap repairs, inpatient rehabilitation, and prolonged hospital stays (greater than four months).

Conclusion: The patient suffered from significant morbidity due to tension pneumocephalus. Concurrent chemoradiation can lead to erythema, edema, and xerostomia acutely as well as hypothyroidism, hypopituitarism, and hearing loss long term. However, the development of pneumocephalus in this case displays a very rare but significant complication which should be discussed with the patient before initiating treatment.
A Case of Suspected Retroperitoneal Fibrosis and Anti-dsDNA Negative Systemic Lupus Erythematosus

Natasha Monga MSIII, Movses Kazanchyan MD, Omar Canaday MD

A 28 year old Hispanic male with no significant past medical history presented with one month of intermittent nausea and nocturia, five days of emesis, one day acute onset lower abdominal pain, and watery diarrhea. He endorsed loss of appetite and fatigue but denied recent weight loss, fevers, chills, changes in diet, sick contacts, or recent travel. He presented to the ED one month earlier with right sided flank pain, thought to be due to nephrolithiasis. A CT at that time demonstrated mild right hydroureteronephrosis associated with right perinephric and periureteral stranding without evidence of stone. He was prescribed NSAIDs, instructed to stay hydrated, and discharged home. Since that hospital visit, he did not recall passing a stone. On this admission, his vitals showed hypertensive urgency but otherwise were within normal limits. Physical exam was significant for tenderness to deep palpation of the medial bilateral lower quadrants, left sided CVA tenderness, bilateral synovitis, and subsequent peripheral edema appearing days after his initial presentation. His CBC and iron panel were consistent with anemia of chronic inflammation, CMP with acute kidney injury, and UA with pyuria, hematuria, proteinuria, and hyaline casts. Abdominal CT on this admission indicated bilateral nephromegaly, areas of increased density in the pararenal space, and bilateral perinephric stranding around the ureters.

During the course of this hospital admission, the patient was started on solumedrol for nephrotic syndrome, furosemide for diuresis secondary to peripheral edema, and lisinopril and clonidine for hypertension management. Within one day of corticosteroid initiation, the patient’s genitourinary and gastrointestinal symptoms resolved. The etiology of his nephrotic syndrome was targeted through labs and kidney biopsy. The patient had a current ANA Titer of 1:640 and a previous ANA titer 1:160 two years earlier. Labs were negative for Anti-dsDNA, Anti-Smith, Hepatitis B, C, HIV, anti-GBM, C-ANCA, P-ANCA, ASO, SPEP/UPEP. His kidney biopsy showed diffuse proliferative glomerulonephritis with crescents, extensive chronic tubulointerstitial disease, and moderate arterial and arteriolar sclerosis.

There are several factors that make this presentation of SLE atypical. Epidemiologically, SLE affects females: males 7-15:1 in the United States. While not impossible, male presentation of SLE is rare in and of itself. Next, this patient only meets criteria for SLE diagnosis by the 2012 Systemic Lupus International Collaborating Clinics Criteria as he had a positive ANA titer and a biopsy consistent with lupus nephritis; he does not meet the classically accepted 1997 American College of Rheumatology Criteria. Additionally, the patient was anti-dsDNA negative at the time of presentation. Although uncommon to be negative for this test, it has been described that ~70% of patients with lupus will test positive for anti-dsDNA at some point in the course of their disease. Lastly the patient’s primary gastrointestinal and genitourinary presentation, imaging showing areas of hyperdensity in the pararenal space, and response to corticosteroids are consistent with retroperitoneal fibrosis. This illustrates the possible autoimmune pathogenesis of this process and the role of autoimmune suppression in treatment for this condition.
NEW JERSEY POSTER FINALIST - CLINICAL VIGNETTE Meghan Nahass

Post Herpetic Neuralgia After Long Thoracic Palsy from Epstein Barr Virus (EBV) Infection

First Author: Meghan Nahass, Rutgers-Robert Wood Johnson Medical School, New Jersey Nahass RG, MD - ID Care, New Jersey

Introduction: A winged scapula occurs with paralysis of the long thoracic nerve and is uncommon. Causes include trauma and viral infections, among others, but EBV has rarely been cited\textsuperscript{i},\textsuperscript{ii}. The development of neuropathic pain after EBV induced mononeuropathy has not been previously reported.

Case Description: A 21 year old female developed fatigue, fever of 103 F, exudative pharyngitis, and lymphadenopathy. The mono spot was positive. Her course was complicated by moderate hepatitis with bilirubin-2.4 mg/dL, Alk Phos-287 IU/L, ALT-441 IU/L, AST-287 IU/L. This was accompanied by a “burning” sensation in the right parascapular area and difficulty raising the arm. A right upper quadrant ultrasound was negative. The burning sensation gradually disappeared, and the patient recovered, however, there was persistent limitation in lifting the right arm. She presented to an orthopedic surgeon two months later and on exam had limited forward flexion to 90 degrees, passive motion with assistance to 155 degrees, and marked winging of the right scapula. A nerve conduction study showed long thoracic nerve abnormalities. Post-viral long thoracic nerve palsy was diagnosed and physical therapy was prescribed. Over the next three years the patient recovered 90% of range of motion but not complete resolution of the winged scapula. The patient also reported occasional episodes of intense “burning” in the right parascapular area that lasted for 1 minute and was associated with temporary limitation in movement of the arm. The episodes resolved without residual symptoms within 5 minutes.

Discussion: Infectious mononucleosis is caused by EBV (Human herpesvirus 4). Although common, it rarely is associated with a winged scapula\textsuperscript{4,5}. The episodes of “burning”, resemble descriptions of post herpetic neuralgias\textsuperscript{iii}, which have been noted after HSV 1 and VZV infections\textsuperscript{iv} but not after EBV. The long thoracic nerve is the sole supplier to the serratus anterior muscle. Nerve injury causes deficits of abduction and elevation of the arm, resulting in a winged scapula\textsuperscript{v}. Diagnosis is made by clinical exam and most cases resolve within 2 years with conservative treatment\textsuperscript{5}. This patient’s acute onset of paralysis of the long thoracic nerve with a winged scapula during an ongoing mononucleosis infection and associated with post herpetic neuralgias 3 years after the insult are a unique constellation of symptoms.

NEW JERSEY POSTER FINALIST - CLINICAL VIGNETTE Brian J Wentworth

Chronic, Cutaneous, and Calcified: Not Your Everyday Ulcer

Brian J Wentworth, Qasim Salimi MD, Julia P Grimes DO MPH

Calcinosis cutis involves the deposition of calcium and phosphorus within the skin, causing a chronic inflammatory state that damages tissue and interferes with calcification inhibitors, facilitating mineralization. Additionally, the deposits may ulcerate, extrude calcium salts, or become secondarily infected. While classically seen in systemic sclerosis and dermatomyositis, calcinosis cutis may rarely present in other autoimmune connective tissue diseases (ACTDs).

A 37 year-old Indian woman with SLE/RA overlap syndrome and GERD presented with non-healing left lower extremity ulcers of 4 months duration unresponsive to cephalaxin and levofloxacin. The ulcers began as raised, erythematous, and painful lesions that initially drained a thick, whitish fluid. Of note, the patient reported a five year history of similar slow-healing ulcers. Extensive rheumatologic workup prior to admission revealed positive or elevated levels of the following: ANA (speckled pattern), anti-Sm, RF, anti-CCP, SS-A, ACE, anti-RNP. A lower-extremity x-ray one year prior revealed subcutaneous calcifications. ROS revealed intermittent fevers, fatigue, dysphagia, arthralgia, morning stiffness, bilateral painful extremity subcutaneous nodules, and Raynaud’s phenomenon. Her medications included omeprazole, sulfasalazine, methotrexate, hydroxychloroquine, prednisone, folic acid, tramadol, and levofloxacin. Family history was significant for maternal RA.

On admission, the patient was tachycardic and physical examination revealed a thin, anxious woman. Neurologic, ophthamlic, cardiac, pulmonary, and abdominal examinations were unremarkable. Musculoskeletal exam was significant for symmetric MCP and PIP joint swelling and ulnar deviation. Dermatologic examination revealed a malar rash, left lower-extremity 2x2 cm and 1.5x1 cm ulcerations to subcutaneous tissue, multiple healed bilateral lower extremity ulcerations, and multiple bilateral extremity <1cm subcutaneous nodules. No oral ulcers, sclerodactyly, telangiectasias, heliotrope rash, or Gottron’s papules were noted. Labs revealed mild leukopenia without neutropenia, anemia of chronic disease, and elevated ESR. The initial differential diagnosis included rheumatoid vasculitis, infection, and pyoderma gangrenosum. Wound and tissue cultures revealed pan-susceptible Pseudomonas aeruginosa. Punch biopsy was performed but results were not immediately available. The patient was continued on levofloxacin, sulfasalazine, hydroxychloroquine, and tramadol. After multiple days, granulation tissue began to form within the ulcers and the patient was discharged with close follow-up. Final biopsy review after discharge by a board-certified dermatopathologist revealed calcinosis cutis with multibacterial infection and lipodermatosclerosis. Although calcinosis cutis is a rare complication of SLE/RA overlap syndrome, it should be suspected in patients with subcutaneous nodules that present with chronic ulcers. The delay in the patient’s diagnosis highlights the importance of a thorough work-up for chronic, slow-healing ulcers in all patients, especially those with ACTDs. While bacterial superinfection may occur, poor response to antibiotics should alert the internist that further investigation with biopsy is indicated, as it provides excellent diagnostic and prognostic information. Furthermore, a tendency towards earlier biopsy may avoid unnecessarily subjecting patients to extended courses of antibiotics, particularly if suboptimal responses are documented.
NEW MEXICO POSTER FINALIST - CLINICAL VIGNETTE Barbara Vidal

Sweet’s Syndrome and Insecticides: A Cautionary Tale

Sweet’s Syndrome and Insecticides: A Cautionary Tale Sweet’s syndrome is a rare condition characterized by fever, neutrophilia, tender erythematous skin lesions and a diffuse neutrophilic infiltrate of the upper dermis(1). Its classic presentation is seen in women ages 30-50 with fever and rash. Etiologies may include medications, malignancies and connective tissue disorders. It typically does not present with neurologic symptoms. We present a case of Sweet’s syndrome with neurological features due to an unusual etiology (insecticide).

A 50 year old Hispanic male with past medical history of alcoholism and heroin abuse presented with a vesiculomaculopapular rash at varying stages of healing along his neck, trunk and upper extremities, and a nontender erythematous papular rash along the extensor surface of the legs for two weeks. Two days prior to admission, he was seen at an urgent care clinic and sent home with Permethrin cream, Allegra, and Bactrim. The following day he applied the cream to his lesions and he rapidly developed periorbital edema and multiple lesion eruptions began to form. He presented to the ED and quickly developed altered mental status. His physical exam was significant for systemic inflammatory response, nonfocal neurological exam, negative guaiac stool and DRE, and umbilication and eschars in many of the papular lesions. Laboratory studies revealed pancytopenia but no evidence of infection. Patient was admitted to the hospital and dermatology and infectious disease consults were obtained. CT and MRI of brain revealed no acute intracranial abnormality.

EEG showed a nonspecific moderate diffuse encephalopathic process and no seizure activity. He tested negative for numerous bacterial, viral, and fungal infections by tissue, wound, blood, urine, and CSF analyses. Subsequent punch biopsies of the lesions were positive for Sweet’s Syndrome. On the 4th day of admission, the patient was able to communicate and informed the medical team he had sprayed Raid, an insecticide, over his body for many days to deter mosquitos. Toxicology concluded the manifestation of Sweet’s Syndrome to be consistent with exposure(2) to permethrin-containing insect repellant, exacerbated by the permethrin cream the patient utilized the day before admission. His mental status improved and he was discharged on the 9th day with topical prednisone and 60 milligrams of oral prednisone(3) to be taken daily tapered by 10 mg weekly over 6 weeks.

This case is unique in not only in the unusual patient characteristics and etiology of Sweet’s syndrome, but as well as the transient encephalopathic component that has been seen only if a few cases(4).

NEW YORK POSTER FINALIST - CLINICAL VIGNETTE Binh T Duong Nguyen

Post operative wound infection caused by rare Streptococcus acidominimus bacteria: a case report

First Author: Binh T Duong Nguyen, Sandipkumar Patel M.D, Manu Bansal M.D, Badem Olga M.D

Introduction: Streptococcus acidominimus, a member of streptococcus viridans group, very rarely causes infections in humans. Its rarity and insufficient availability of literature have obscured the diagnosis and management of Streptococcus acidominimus associated infection.

Case description: We report a case of 69 years old male admitted with S. acidominimus associated severe sepsis due to wound infection after laparotomy. Patient was diagnosed with mesenteric ischemia during the previous admission and had undergone right hemicolectomy and ileostomy procedure. The patient had a complicated course after surgery, and was eventually discharged after 10 days of hospitalization. However he was re-admitted in three days with moderate abdominal pain and purulent discharge from the laparotomy wound site. The patient was hypothermic (T°=34.9°C/94.82°F), tachycardic (heart rate of 107/min), with blood pressure of 102/75 mmHg. Laboratory results showed leukocytosis with left shift (WBC 11400/µl, neutrophils 67.5%), lactic acid of 3.0 mmol/l (normal range 0.5-2.2); acute kidney injury, BUN 47mg/dl (normal range, 6-20), creatinine 3.9 mg/dl (normal range, 0.9-1.3), electrolyte imbalance. Wound culture with antibiotics susceptibility showed the growth of mixed bacterial flora, including S.acidominimus susceptible only to Clindamycin. We treated patient with Clindamycin for 10 days. The patient’s wound purulent drainage stopped and the wound was healing well. The patient was discharged clinically stable after a week, with a normal WBC count of 4480/µl, lactic acid of 1 mmol/l, BUN of 9 mg/dl, and Cr of 0.7 mg/dl.

Discussion: Streptococcus acidominimus, a gram-positive coccus, is mostly known to cause variable infections in cattle. Since the first case of pneumonia and pericarditis reported in 1988, until present, the literature review reported 13 patients with different infections due to S.acidominimus. Eight of them were community-acquired infection. The other five happened in hospital settings. In all case S.acidominimus showed different antibiotics susceptibility patterns. This may pose a challenge to proper choice of antibiotic treatment. This case, being the sixth reported where S.acidominimus caused a nosocomial infection, has emphasized the potential of S.acidominimus to cause a life-threatening condition in humans. Our case is the first one to show that nosocomial S.acidominimus can cause severe sepsis with end-organ damage. The striking difference in antibiotics susceptibility of this case highlights that it is necessary to identify the species early for effective clinical management.
NEW YORK POSTER FINALIST - CLINICAL VIGNETTE Thomas A Franzon

THE UNMASKING OF AUTOIMMUNE DISEASE IN PREGNANCY

Thomas Franzon, Arunpreet Kahlon, MBBS, Amit S Dhamoon, MD

Introduction: Thrombocytopenia is found in 7-8% of all pregnancies. The mechanism for thrombocytopenia in pregnancy is most often secondary to an increased activation or destruction of platelets, such as in gestational thrombocytopenia, preeclampsia, and rarely, immune thrombocytopenic purpura (ITP). We present a rare case of thrombocytopenia in a post-partum female.

Case: A 26 year old female gravid 2 para 2 with a history of preeclampsia presented to the hospital two weeks after delivery, with progressively worsening arthralgias involving the small joints in her hands, wrists, elbows, knees, and ankles bilaterally. She reported fevers, malaise, and swelling of her joints that she treated with ibuprofen at home. She denied morning stiffness, but reported some bruising on her toes, right knee, and a few episodes of epistaxis.

Her vital signs were within normal range. A detailed physical exam revealed point tenderness of the small joints in her hands, wrists, elbows, knees, and ankles bilaterally. There was minimal bruising of her right knee and great toes bilaterally. Her lab workup revealed anemia and thrombocytopenia. A hematologic workup revealed elevated LDH, low haptoglobin, normal fibrinogen, and normal ADAMTS13 activity. Direct and indirect Coomb’s tests were negative and a peripheral blood smear did not show evidence of schistocytes.

Rheumatologic work up showed elevated antinuclear antibody, anti-dsDNA, anti-smith, anti-RNP, anti-scl-70, and anti-histone levels and low C3 and C4 complement levels. The patient was diagnosed with ITP secondary to systemic lupus erythematosus (SLE). Her platelet count subsequently improved with steroids and the patient was discharged on prednisone with close rheumatological follow up.

Discussion: Most causes of thrombocytopenia during pregnancy are due to gestational thrombocytopenia, preeclampsia, or ITP. Although the pathophysiology of ITP is not completely understood, the destruction of platelets is related to specific IgG autoantibodies directed against platelet membrane glycoproteins such as Gllb/IIIa. The majority of ITP (80%) is primary and is not associated with a precipitating condition. Secondary ITP is associated with a precipitating condition such as autoimmune disease, viral illness, or malignancy. SLE has been attributed to 2-5% of all cases of ITP. This patient likely experienced a pregnancy-induced flare-up of SLE, causing her thrombocytopenia and arthralgias. The hormonal and biochemical changes during pregnancy are thought to exacerbate lupus, sometimes causing a patient’s first presentation of lupus. SLE should be included in the differential diagnosis of ITP, especially in the pregnant and post-partum female.
NORTH CAROLINA POSTER FINALIST - CLINICAL VIGNETTE Joshua Rivenbark

When Labs and Images Disagree: A Diagnostic Challenge for Progressive Multifocal Leukoencephalopathy

First Author: Joshua Rivenbark Second Author: Cara O'Brien, MD

Introduction: Progressive multifocal leukoencephalopathy (PML) is a rare disease of patients with HIV/AIDS or otherwise compromised immunity. Its rarity and non-specific symptoms make diagnosis challenging and dependent on correlation of clinical, radiologic, and laboratory studies.

Case Report: A 41-year-old gentleman with untreated HIV/AIDS presented with six months of progressive weakness with two days of multiple falls. He also reported progressive cough, fever, chills, nausea, vomiting, and increasing dyspnea. Examination revealed normal vital signs, temporal wasting, diffuse abdominal tenderness, decreased strength in proximal lower extremities bilaterally, and a shuffling gait. Laboratory analysis revealed a CD4 count of 1, and CSF had normal levels of glucose, protein, and nucleated cells. Non-contrasted head CT demonstrated diffuse cerebral atrophy and a white matter hypodensity in the posterior parietal lobe. CSF PCR for JC virus DNA was not performed. A working diagnosis of PML vs. HIV encephalopathy was made. His diffuse weakness persisted unchanged until hospital day 7, when he had a seizure. The seizure was terminated with IV lorazepam; however, he remained unresponsive. EEG showed diffuse slowing, and MRI brain demonstrated a focal region of T1-low, T2-high signal within the right parietal lobe extending to subcortical white matter, consistent with PML. The remainder of his hospitalization was complicated by recurrent seizures and continued unresponsiveness. PCR for JC virus DNA in a stored CSF sample returned negative. Nevertheless, his clinical presentation and imaging findings were sufficiently convincing of PML, and he was discharged to hospice.

Discussion: Despite significantly decreased prevalence in the antiretroviral therapy era, PML still accounts for 3-5% of deaths in patients with AIDS. It can be a challenging diagnosis because of the vague nature of presenting symptoms, further complicated by the impressive differential that often arises in severely immunocompromised patients. Common presenting symptoms of PML include cognitive defects, motor weakness, gait abnormalities, and speech disturbances. Seizures are a less common presenting symptom, but they become more prevalent with disease progression and can help narrow the differential. Diagnosis of PML is typically made without biopsy, through the combination of suggestive clinical features, compatible imaging findings, and detection of JC virus DNA in the CSF. Although specificity of PCR for JC virus DNA in PML approaches 100%, sensitivity is about 75% without using new ultrasensitive techniques. Consequently, a negative PCR test does not rule out PML, and the diagnosis hinges on clinical context and imaging studies to eliminate other possible etiologies. Management of probable or definite HIV-associated PML is centered on correction of immune deficiency; however, mortality approaches 50% at 1 year, and severe neurologic dysfunction is common despite antiretroviral therapy.
Atypical Tularemia Presentation with Primarily Gastrointestinal Symptoms

Justin Shipman

A 43 year old male sought medical care on June 9th with a constellation of symptoms including fever, vomiting, cough, and severe diarrhea. On the day of admission, he had begun to suffer from orthostasis. He was considered as part of a cluster of family members who presented with similar symptoms after being involved in a community clean-up day on May 29th. Specifically, these family members were exposed to urine and animal feces that others involved in the clean-up were not. Physical exam findings included decreased air flow in the lungs bilaterally, diffuse abdominal pain with no hepatomegaly, and a large lymph node on the side of his neck. Laboratory data showed elevated WBCs and liver enzymes, hyponatremia, and hypokalemia. Chest x-ray revealed patchy opacities bilaterally, right perihilar infiltrates, and blunting of the right costophrenic angle. Emperic therapy with doxycycline, metronidazole, piperacillin/tazobactam, and amphotericin was started to cover likely bacterial organisms. Tests for infectious diarrhea included c. difficile, legionella, giardia, cryptosporidium, salmonella, shigella, campylobacter, e.coli, aeromonas, norovirus, and yersinia. A hepatitis panel and HIV antigen testing were also done due to the patient’s past history of drug use. All tests came back negative. During this time, empiric treatment was switched to vancomycin, ciprofloxacin, and piperacillin/tazobactam via recommendation by infectious disease. Further laboratory testing was done for tularemia, q fever, leptospira, rotavirus, and adenovirus. All tests came back negative, except for tularemia which had a titer of 1:40. Further testing was done a month later and the titer was 1:2560, which was considered diagnostic for tularemia. The patient spent a total of 10 days in the hospital. His nausea, fever, and diarrhea slowly improved and he was discharged after these symptoms had resolved. One month after admit, he continues to have headaches and remains 30 pounds below his pre-sickness weight due to the severe diarrhea and loss of appetite caused by tularemia.

This case illustrates the severity and variability of symptoms that can be present in a patient with tularemia. Not only did this patient have an unusual presentation with primarily gastrointestinal symptoms, but he was also outside the typical geographic areas for tularemia. This case represents the importance of maintaining a broad differential in order to diagnose a disease that is presenting in an uncharacteristic pattern and geographical region.
OHIO POSTER FINALIST - CLINICAL VIGNETTE Megan Caroway

Elevated PTT as a clue to undiagnosed adnexal masses

First Author: Megan Caroway Faculty Author: LeAnn Coberly, MD

Case description: A previously healthy 83 yo female presented with hematuria. She was known to have adnexal masses of unknown etiology discovered by CT imaging six years ago for which she declined work up. She had no prior history of bleeding and there was no family history of bleeding disorders or autoimmune disease. Physical exam revealed grossly bloody urine with clots. Urine culture and cytology were normal. Laboratory studies were normal with the unexpected finding of an isolated elevation in the PTT. Lupus anti coagulant was not present.

A mixing study did not correct with addition of control plasma confirming the diagnosis of an inhibitor. Further studies revealed a FVIII activity level of less than 1% with a high Bethesda Titer of 96 BUs. The Bethesda assay quantifies the concentration of inhibitor present with 1 BU representing the amount of inhibitor required to neutralize 50% of the FVIII. A titer of at least 5 BUs indicates the presence of an inhibitor. This patient was treated with recombinant factor VII, Rituximab, Cytoxan and prednisone resulting in cessation of hematuria. Discussion: Acquired hemophilia is a rare disorder with an incidence of about 1 per million cases occurring yearly. FVIII inhibitors are often associated with severe morbidity and mortality making it an important diagnosis to recognize to ensure prompt initiation of therapy. FVIII inhibitors are immunoglobulins produced in the setting of immune activation and are classified as alloantibodies or autoantibodies. Alloantibodies form in response to exogenous FVIII exposure and autoantibodies form in the setting of autoimmunity or malignancy.

The latter interferes with the interaction between FVIII and von Willebrand factor and FVIII cleavage sites. Treatment addresses acute bleeding and eradication of the autoantibodies. Bypassing agents increase FVIII to stop acute bleeding. The most frequently used agents include recombinant FVII, activated prothrombin complex concentrates (aPCC), and desmopressin. Inhibitor removal requires immunosuppressive or cytotoxic agents. Corticosteroids and cyclophosphamide are the most well studied and widely used. Complete eradication of the inhibitor occurs in about 70-80% of patients with an average of 5 weeks of treatment. Those with higher titers of inhibitor often have a protracted course or require second line therapy. The etiology of this patient’s inhibitor was likely due to presumed malignancy suggested by the adnexal masses present on imaging. The patient is currently on daily prednisone with no recurrence. Conclusion: Increased awareness of acquired hemophilia may prompt further investigation into the effectiveness of alternative treatment options since current therapies are costly and with serious side effects.
PULMONARY ARTERY SARCOMA MASQUERADING AS PULMONARY THROMBOEMBOLISM

Jessica Dreicer (student) and Jean M. Elwing, MD, FCCP, University of Cincinnati Academic Medical Center, Cincinnati, Ohio.

Case Presentation: A 44-year-old female with a history of recurrent DVTs and pulmonary emboli (PE) on warfarin and status post-IVC filter presented with acute on chronic dyspnea. Dyspnea occurred with any level of exertion without corresponding desaturation. The patient had unintentionally lost 40 lbs in the past three months and had evidence of anemia of chronic disease and elevated inflammatory markers. CT pulmonary angiogram revealed chronic large filling defect in the left main pulmonary artery concerning for pulmonary thromboembolic disease. In light of the consistently elevated inflammatory markers and recent weight loss, there was concern for a malignancy as the etiology for her recurrent thromboembolic disease. Due to the magnitude of the clot and her chronic dyspnea, the patient underwent pulmonary artery endarterectomy (PEA). During the procedure, surgeons found a near complete obstruction of the left pulmonary artery by embolus and a firm mass adherent to the arterial wall. Pathology demonstrated low-grade myofibroblastic sarcoma. Left pneumonectomy was performed as definitive treatment. At 6 years, a defect in the right pulmonary artery raised concern for recurrence however the defect was PET negative and repeat CT scan at one year was stable. The patient has had long-term survival of 73 months without recurrence or metastasis.

Discussion: Pulmonary artery sarcoma (PAS) is a rare malignancy with approximately 300 case reports since 1923. Survival is poor, reported in the literature as 6.6-144 months with a mean of 12. Histology appears to correlate directly with survival. Those surviving greater than three years have tumors with low-grade myofibroblastic features.

The mainstay of treatment for PAS is surgical. Both resection and pneumonectomy are utilized but long-term survival is reported only after pneumonectomy. This patient is status post pneumonectomy with survival of 73 months, considerably longer than the average reported survival. Typical symptoms of PAS are identical to those of pulmonary thromboembolic disease including dyspnea and chest pain. PAS is a luminal tumor that forms nodules and plaques in the direction of blood flow making it appear similar to PE on CT. This extensive overlap complicates the diagnosis of this rare malignancy; PAS is seldom diagnosed pre-operatively. Up to 3-4% of patients undergoing PEA are found to have primary sarcomas.

FDG PET/CT is emerging as a methodology to distinguish PAS from PE. A study directly comparing PAS and PE found that PAS is frequently FDG avid, while PE is not. This methodology was used to evaluate concern for this patient’s recurrence. Exploiting this distinction could allow for evaluation of possible recurrence or earlier detection of PAS and thus improve patient outcomes.
Hemolytic anemia in a patient with triple valve repair

First Author: Teresa A Evans PhD Senior Author: Clifford Packer MD

Introduction: Hemolysis after valve replacement due to shear forces is well documented with single and double (aortic and mitral) valve replacement (review, Mezozi 2002) and with annuloplasty ring valve repair (Ishibashi 2005). The median interval from valve replacement to presentation of hemolytic anemia is three months in single valve replacements (review, Shapira 2009). Hemolysis after triple valve repair is poorly described except for a case study using mechanical valves improved by replacement with bioprosthetics (Camishion 1979).

Case Presentation: A 57 year old African American man presents with fatigue and intermittent black stools. He has an extensive past medical history including congenital solitary right kidney, end stage renal disease, hemodialysis with erythropoietin, Hepatitis C, coronary artery disease, heart failure with an EF of 20-25% and triple cardiac valve repair three months ago with a 29 mm Biocor mitral bioprosthetic valve; a 23 mm Trifecta aortic bioprosthetic valve and a 31mm tricuspid Duran Annuloplasty ring. He presented with a four day history of intermittent black stools, abdominal fullness, a positive hemoccult and a hemoglobin of 5.8. He takes Coumadin and aspirin, but denies any recent NSAID use. A colonoscopy three months previous showed only internal hemorrhoids. He received a transfusion of two units of PRBCs, his hemoglobin incrementing appropriately to 8.1. He underwent a EUGD, which showed no evidence of bleeding. No further evidence of GI bleeding was found and black stools resolved.

His complete blood count showed a white count of 8.6, with differential notable for 8.6% monocytes and 3.5% eosinophils. His reticulocyte count was 7% and RDW was 23.2. Folate and ferritin levels were increased. LDH was 930. Haptoglobin was <6%. PTT was 36.2. TIBC, iron, fibrinogen and factor V activity were normal. His blood smear was normal immediately after transfusion. Two days later 4% schistocytes were found, increasing to 15% four days after transfusion. Hemoglobin dropped from 8.1 to 7.3 to 7.0 at two day intervals after transfusion. Only occasional spherocytes and target cells were observed. Burr cells were present, likely due to artifact or dialysis. Three days after transfusion LDH was 1084 and haptoglobin <6%. This prompted a transthoracic cardiac echo showing three bioprosthetic valves with moderate to severe paravalvular leaks and moderate tricuspid regurgitation. This patient with multiple comorbidities was managed with erythropoietin and transfusion.

Discussion: Diagnosis of hemolysis in patients with multiple possible causes of anemia can be challenging and multiple testing modalities required. Hemolysis after triple valve repair can be significant, although contribution from individual valves is difficult to isolate. Management typically consists of revision surgery or erythropoetic stimulating drugs and trans-catheter repair approaches to close paravalvular leaks in poor surgical candidates.
Primary vaginal melanoma: An incidental finding on routine pelvic examination

First Author: Ryan Loreno Lym, Medical Student, Case Western Reserve University School of Medicine, Cleveland, OH Second Author: Debra Leizman, MD, FACP, Assistant Professor, Case Western Reserve University School of Medicine, Cleveland, OH

Introduction: Primary vaginal melanoma is a rare and aggressive cancer. It accounts for less than 3% of vaginal cancers and less than 1% of malignant melanomas with an incidence of 0.26/10,000 women per year. Five-year survival rate ranges from 10-20% and there is no effective treatment. UV radiation is not the causative factor and its etiology is unknown. Workup requires pelvic examination of a vaginal lesion with biopsy and histopathological diagnosis.

Case: A 79-year-old woman with a history of endometrial carcinoma status post total hysterectomy in January 2013 was found to have a vaginal lesion in January 2014 on a routine pelvic exam. The exam was done according to current PAP smear guidelines for a patient whose hysterectomy was performed for endometrial carcinoma. The lesion was biopsied and determined to be primary vaginal melanoma. It was excised and initial staging showed no evidence of metastasis.

A follow up pelvic exam in March showed recurrence of three separate vaginal lesions that demonstrated recurrent melanoma. They were excised and PET-CT showed no distant metastasis. She subsequently completed whole pelvic radiation but in July a staging CT scan showed a lesion in the left lung that was confirmed to be metastatic melanoma. The patient was then put on Ipilimumab therapy.

In September she was admitted for complaints of dyspepsia, diarrhea, headache, and dyspnea concerning for progression of metastatic disease and Ipilimumab toxicity. EGD demonstrated erosive gastritis secondary to NSAID use. Bowels were positive for Clostridium Difficile and she was treated with metronidazole. CT scan showed diffuse metastases to the lung, liver, and pancreas. Brain metastasis was confirmed with volumetric MRI. Thoracentesis with subsequent PleurX placement was performed in an effort to relieve the dyspnea felt secondary to the diffuse lung metastases and malignant pleural effusion. Upon discharge it was established that she had failed Ipilimumab therapy and possible options for future management included gamma knife radiation with considerations for hospice and palliative care.

Discussion: Current guidelines recommend against pelvic exams in low risk women such as those older than 65 with adequate screening history or in those who have had a total hysterectomy for benign reasons. However, this case illustrates the importance of follow up pelvic exams in high-risk individuals. For this patient, despite her age and total hysterectomy, her history of endometrial carcinoma and primary vaginal melanoma prompted the need for post-treatment surveillance by pelvic exam. Her exams were important in detecting the presence of her primary vaginal melanoma and its recurrence.
Fusobacterium nucleatum: a rare cause of hepatic pyogenic abscess

First Author: Dhruvika Mukhija Second Author: Sajan Jiv Singh Nagpal Third Author: Preethi Patel

Introduction: Fusobacterium nucleatum is an anaerobic oropharyngeal bacterium that typically causes periodontal disease and was first recognized due to its association with Lemierre’s syndrome i.e. septic thrombophlebitis of the neck vessels secondary to oropharyngeal infection. Rarely, Fusobacterium can also cause visceral abscess formation with or without accompanying visceral thrombophlebitis.

Case Description: A 69 year-old female presented with a 2-month history of vague right upper quadrant (RUQ) pain and intermittent fevers and chills. She had a past medical history significant for emphysema, type II diabetes mellitus, benign pancreatic and renal cysts and an infra-renal abdominal aortic aneurysm (AAA) repair five months prior to presentation. Physical exam revealed poor dental hygiene and moderate RUQ tenderness in an otherwise soft abdomen with no rigidity or guarding. Murphy sign was negative. Ultrasound imaging of the RUQ revealed a 9x7x7 cm hypoechoic density in the right hepatic lobe, consistent with a pyogenic liver abscess. Abdominal computerized tomography (CT) showed a multiseptated thick walled abscess-like mass in the right hepatic lobe and no other abscesses or potential sources of infection. After blood cultures were drawn, the patient was started on broad spectrum antibiotic coverage with Vancomycin and Meropenem. CT guided pigtail drain placement was then performed. Cultures from the drain fluid as well as admission blood cultures remained negative initially but after prolonged incubation (Day 6 and Day 10 for drain and anaerobic blood cultures respectively), revealed Fusobacterium nucleatum. She was evaluated by dentistry who found radiological evidence of moderate to severe chronic periodontitis for which she underwent extraction of all remaining teeth. She improved clinically and was eventually discharged home on intravenous Ertapenem to complete a total of two weeks of intravenous antibiotic therapy, followed by a four week suppressive regimen of oral Penicillin VK. Prior to discharge, an endoscopic ultrasound (EUS) guided pancreatic fine needle aspiration was negative for malignant cells in the pancreatic cystic lesion. Repeat CTs at two and four months post discharge showed complete resolution of the hepatic lesion.

Discussion: Besides liver abscess, differential diagnoses for a liver hypodensity can include primary (hepatocellular) or metastatic malignancy (especially colon adenocarcinoma) and vascular malformations. Since the suspicion for infection was really high in this case, it was decided to pursue CT guided drain placement with cultures incubated for an extended period. Fusobacterium sp. are an extremely rare cause of liver abscess with only about 20 cases described so far, most of which are in immunocompromised hosts. Fusobacterium sp. should be considered as a possible cause of pyogenic liver abscesses, especially in patients with poor dental hygiene.
Discussion: Kaposi sarcoma is a vascular tumor that is commonly associated with human herpes virus 8. It is one of the most common tumors in AIDS patients. Its incidence has been significantly reduced to 6 cases per million people per year due to ART. It typically presents as cutaneous lesions and rarely spreads viscerally due to ART. When there is visceral involvement, it most frequently spreads to the oral cavity, gastrointestinal tract, and the respiratory system. Chest CT and x-ray imaging will typically show central peribronchovascular opacities and nodular densities. Biopsy will reveal Kaposi sarcoma lesions that exhibit spindle cells surrounding small vascular channels. Once the diagnosis has been made, the patient should be started on ART, which has been shown to significantly improve the prognosis.

Pulmonary Kaposi sarcoma presents nonspecifically. Its symptoms can often be confused with other infectious etiologies that commonly occur in HIV/AIDS patients. If a thorough infectious workup with appropriate antibiotic treatment fails to resolve respiratory symptoms in this patient population, Kaposi sarcoma with visceral involvement should be considered. A careful search for skin lesions suggestive of Kaposi sarcoma and evaluation with bronchoscopy should be performed.
Not All That Wheezes is Asthma

First Author: Madeleine Strohl Second Author: Clifford Packer

**Introduction:** Tracheal stenosis is a rare complication following brief (less than one week) endotracheal intubation. It is commonly misdiagnosed as an asthma or COPD exacerbation, which results in delayed diagnosis and treatment. We report here on a case of severe tracheal stenosis following a 72-hour intubation that was initially misdiagnosed as an asthma exacerbation.

**Case Report:** A 52-year-old female with a five-pack-year smoking history was admitted to the hospital with persistent shortness of breath and wheezing of two weeks duration following an upper respiratory infection. Her medical history was notable for GERD, bipolar II disorder, and a recent 72-hour intubation for hypoxic respiratory failure secondary to a drug overdose two months prior. She was prescribed an albuterol inhaler for seasonal allergies. Pulmonary function tests from five years prior were normal but a methacholine challenge was not performed at the time. Her symptoms included shortness of breath that worsened on exertion, wheezing and a dry cough. She was now using her albuterol inhaler four times a day with some relief of her symptoms. During her admission to the hospital, she was given albuterol and ipratropium nebulizers and discharged to home to complete a five day course of prednisone after moderate improvement in her dyspnea. She returned to the emergency department five days later when her symptoms persisted.

On physical exam, her temperature was 36.8°C, heart rate 86, respiratory rate 16, blood pressure 124/84 and oxygen saturation of 95% on room air. Lung auscultation revealed mild bilateral expiratory wheezes and stridorous breath sounds on exertion. The rest of her physical exam was unremarkable. Her complete blood count and renal function panel were within normal limits. Her chest radiograph was normal. On spirometry, her FVC was 2.86 (85% of predicted), FEV1 was 0.59 (22% of predicted) and FEV1/FVC was 21%. Her flow-volume loop demonstrated marked limitation of the inspiratory and expiratory flow, consistent with a fixed obstruction. Flexible laryngoscopy revealed 80% tracheal stenosis at the third tracheal ring. Computer tomography (CT) of the chest and neck with contrast confirmed the presence of a stenosis in the mid trachea with an area of 6mm by 3mm. She was continued on albuterol and ipratropium nebulizers and restarted prednisone with mild improvement of her symptoms. She was transferred to a tertiary care center for tracheal resection by cardiothoracic surgery.

**Discussion:** The diagnosis of tracheal stenosis should be considered in patients with a recent history of intubation who are presenting with new or worsening respiratory symptoms. Additionally, the value of fundamental lung auscultation skills should not be underestimated. Knowing the clinical difference between wheezing and stridor can aid in making the right diagnosis and expediting the correct management.
Leukocytoclastic vasculitis following influenza vaccination

First Author: Sissi Cao BSc, MD (c) Dongmei Sun MD, MSc, FRCPC

Case Description: A 60-year old man presented with an extensive rash and fever to the emergency room five days after receiving his annual influenza vaccine. He developed chills and diffuse joint pain that same evening and noticed the rash appearing on his hands first before spreading to his limbs and trunk the next day, along with a fever of 102 Fahrenheit. His past medical history was significant for a 3-year history of interstitial pulmonary fibrosis.

His only medication was N-acetylcysteine, which he had been taking for 1 year. He had a 30-pack year history of smoking but stopped one year ago and was home oxygen-dependent for 10 months. There were no sick contacts or travel. Upon examination, his vital signs were stable. He had a mild fever of 99.7 Fahrenheit. There was an erythematous urticarial macular rash with mucosal sparing involving the face, trunk, bilateral hands, arms, thighs and feet. There was striking palmar erythema and periungual hemorrhage on the fingers and toes. Blood work showed leukocytosis of $15.8 \times 10^9/L$ (4.0-10.0), an elevated C-reactive protein of 200 mg/L (5.0) and elevated liver enzymes. He was treated with oral hydroxyzine and 50 mg prednisone daily for one week. A full vasculitis work-up was negative for c-ANCA, p-ANCA and ANA antibodies with normal complement and negative cryoglobulin levels. Serology was negative for acute infection with HAV, HBV, HCV, EBV, CMV and parvovirus B19. Urine microscopy and stool cultures were negative. Skin biopsy showed leukocytoclastic vasculitis. On follow up at 10 days after initial presentation, leukocytes had returned to normal and the skin on his face, trunk and legs was dry and beginning to slough.

Discussion: Annual influenza vaccination is the most important way to prevent seasonal influenza viral infections and severe complications, including death [1]. Most reactions to vaccination are mild and self-limiting; hypersensitivity reactions to vaccine components and Guillain-Barre Syndrome are rarely reported [1]. More than 30 reported cases of vasculitis post-influenza vaccination have been reported since 1974 with 7 being cases of leukocytoclastic (cutaneous) vasculitis, a small-vessel vasculitis caused by nuclear debris from infiltrating neutrophils [2]. A possible mechanism for the link is an immune-mediated response to viral antigens or vaccine excipients [2]. Reported patients consistently are elderly or have chronic illness, and most have a complete response to steroid therapy and favorable outcomes. In North America, influenza vaccination coverage is trending upwards [1]. In current practice, acute illness is screened for prior to vaccination. However, while the influenza vaccine is highly safe and effective, clinicians should be aware of the possible association between vaccinations and cutaneous vasculitis in patients with chronic disease [1].

References:
Effective outpatient management of denosumab-induced hypocalcemia in a long-standing hemodialysis patient.

First Author: Sissi Cao BSc, MD(c) Elizabeth Froats RN, Lisa-Ann Fraser MD, MSc

Case Description: A 58-year old man with chronic kidney disease (CKD) on hemodialysis was referred for skeletal evaluation. He had a history of chronic prednisone use and multiple fragility fractures including: several vertebrae, pelvis, bilateral hips, left scapula, right humerus, and a spontaneous fracture of his right jaw while chewing food. Investigations revealed a serum calcium of 2.16 mmol/L (2.15-2.60), albumin 40 g/L (40-50), PTH 24.4 pmol/L (1.3-8.2), 25-OHvitD 126 nmol/L (75-225) and C-telopeptide 1541 ng/L. His CKD-metabolic bone disease was being managed with cinacalcet (40 mg daily) and vitamin D3 (2000 IU daily). He was diagnosed with severe osteoporosis and started on denosumab (60 mg).

After his initial injection, bloodwork was arranged to monitor for hypocalcemia. By post-injection day 8, he had developed profound hypocalcemia with a serum calcium of 1.59 mmol/L. He experienced only minor acral paresthesia, with no cramping or tetany. One gram of intravenous calcium gluconate was given acutely, and aggressive outpatient management was arranged. His cinacalcet was discontinued and he was started on calcitriol (0.25 mcg TID), oral calcium carbonate (1 gram QID), and extra calcium (14.9 grams) was added to his hemodialysis bath (2.5 hrs, 5 days per week). Follow up bloodwork was arranged every 2 days during dialysis to monitor progress. Within 20 hours, his serum calcium had risen to 2.11 mmol/L and remained stable. On day 19 (calcium 2.46 mmol/L) his calcitriol was tapered to BID, then further reduced on day 23 (calcium 2.12 mmol/L) to OD. On day 35 (calcium 2.12 mmol/L) all calcitriol and extra calcium were discontinued, and he restarted his cinacalcet and vitamin D3 without issue.

Discussion: Denosumab is an osteoporosis medication highly effective at reducing bone turnover, thereby reducing fracture risk. Not dependent on renal clearance, denosumab is currently the only osteoporosis agent considered safe in the setting of significant renal dysfunction. However, hypocalcemia has been documented as a side effect in CKD patients, and may be particularly severe in those on dialysis [1]. To date there have been 12 reported cases of hypocalcemia following denosumab use in dialysis patients. The timing and severity of the hypocalcemia varies; several reports detail rapidly reaching a nadir calcium concentration within 16 days of injection, similar to our patient [2,3]. Resolution and reported return to baseline of calcium values varies, ranging from 91 to 139 days [2,3]. We anticipated possible problems with hypocalcemia in our patient and therefore arranged bloodwork one week following initial denosumab injection. Our patient demonstrates how, with routine post-injection bloodwork and careful alteration of medications, dialysis patients can safely receive denosumab without undue suffering or the need for hospitalization.

References:
OREGON POSTER FINALIST - CLINICAL VIGNETTE Karen Bieraugel

Cat Got Your Spleen? A Case of Hepatosplenic Bartonella Infection

First Author: Karen Bieraugel, BA Andrew Oehler, MD Megan NeSmith, MD Joseph Chiovaro, MD

Introduction: Cat scratch disease (CSD) can present a diagnostic challenge, especially when it manifests in an atypical format. We report a rare presentation of CSD as hepatosplenic disease in an immunocompetent adult.

Case Description: A 63-year-old goat herder presented with three weeks of recurrent intermittent fevers accompanied by fatigue and a 22-pound unintentional weight loss. He endorsed only mild headaches and arthralgias, without any myalgias, rashes, lymphadenopathy, abdominal pain, conjunctivitis, or seizures. His past medical history was notable solely for latent tuberculosis, treated with nine months of isoniazid 30 years prior. He owned numerous dogs and semi-domesticated cats, including at least 18 kittens in the past year. He did not recall any recent animal bites or scratches. On presentation, he was febrile but otherwise hemodynamically stable. His physical exam was notable only for pertinent negatives including lack of hepatosplenomegaly, lymphadenopathy, rashes, or murmurs. Results from his liver function and basic metabolic panel were within normal limits. His white blood cell count was 12.5 cc/mm, with 90% neutrophils. ESR and CRP were mildly elevated. A CT scan of the chest, abdomen, and pelvis revealed multiple liver and splenic hypodense lesions. Liver biopsy demonstrated mixed inflammatory infiltrate with giant cell histiocytes but no well-formed granulomas. Stains for infectious organisms were negative. After several days of hospital observation with recurrent fevers, Bartonella henselae IgG and IgM titers returned positive at >1:1024 and >1:320, respectively. A diagnosis of hepatosplenic CSD was made. The patient was treated with Doxycycline and Rifampin for 4 months. By two weeks into the treatment course, the patient’s fevers had subsided. Two months from the start of treatment, his Bartonella henselae IgM titer was undetectable (<1:20), while IgG titer remained >1:1024.

Conclusion: Cat scratch disease is primarily a disease of the pediatric population, with most patients presenting with self-limited local lymphadenitis. Hepatic involvement in CSD is well described in the immunosuppressed as peliosis hepatis, but has only rarely been reported in immunocompetent adults. Diagnosing hepatosplenic cat scratch disease is challenging. Patients may not report cat exposure or scratches, and there are few clinical clues that distinguish cat scratch disease from other multifocal hepatosplenic processes. Additionally, there is no definitive serologic, microbiologic, and pathologic test for CSD.

We review the epidemiology, clinical manifestations, diagnosis, and treatment of this rare, yet important, clinical entity. This patient’s infectious exposures, abdominal imaging, and eventual positive Bartonella henselae serologies confirmed the unusual diagnosis of hepatosplenic CSD. This case stresses how multisystem involvement, inaccurate diagnostic testing, and the plurality of rare presentations make the diagnosis of CSD challenging and costly.
OREGON POSTER FINALIST - CLINICAL VIGNETTE Herman "Marty" Martin

When Deference to Expertise Causes the Primary Provider Chest Pain

First Author: Herman "Marty" Martin, MA Cassandra Betts, MD, Renee Segura, MD

Methamphetamine is known to induce coronary artery vasospasm and increase myocardial demand, triggering or accelerating coronary artery pathology, leading to acute coronary syndrome (ACS). The challenge of identifying the relative contributions of atherosclerotic vs. drug-induced coronary pathology in patients with ACS requires close attention to potential cognitive biases that may arise as well as consideration of the patient’s broader medical picture. General medicine teams and consultants alike must be diligent to interpret their patient’s subjective and objective presentation comprehensively and without bias.

A 57-year-old gentleman with a history of hypertension, family cardiac history, type 2 diabetes, tobacco use, and past history of methamphetamine use was admitted following 2 weeks of atypical chest pain and dyspnea. Several months prior to admission, he underwent a myoview stress test negative for obstruction or ECG changes. He reported methamphetamine use three days prior to admission after 10 years of abstinence. Non-ST elevation MI (NSTEMI) was diagnosed due to elevated initial troponin and ST/T-wave abnormalities. These abnormalities included biphasic T-waves in leads V1-V4 consistent with Wellens’ sign, suggestive of proximal left anterior descending (LAD) stenosis. Cardiology was consulted and concluded that, in light of his recent negative myoview, his meth use caused increased demand and vasospasm leading to myocyte injury and type 2 NSTEMI. The primary team maintained suspicion of underlying coronary artery disease given the patient’s symptom onset prior to drug use and multiple CAD risk factors. When an echocardiogram revealed wall motion abnormalities in the LAD territory consistent with ECG findings, the primary team readdressed their concerns with the consultants and advocated for cardiac catheterization. The patient underwent catheterization, showing 99% stenosis of the mid-LAD coronary artery and a non-obstructive plaque causing moderate stenosis of the left circumflex artery. Balloon angioplasty was performed with bare metal stenting.

This case illustrates the challenges a primary team faces in managing complex care in a broad discipline. Medicine teams are charged with advocating for their patients and prioritizing input from specialists with their own biases and incomplete views of the patient. With ACS patients, it is important to recall Wellens’ sign and that methamphetamine not only causes vasospasm but also accelerates atherosclerotic disease. Anchoring bias, the tendency to rely too heavily on an initial or prominent finding of a case, was evident in the consultants’ focus on the patient’s recent meth use and negative myoview despite data arguing for an alternative interpretation. This cognitive bias influenced the consultant’s perspective, requiring the primary team to carefully consider expert opinion in the broader patient context.
Diffuse lymphadenopathy and weight loss of unkown etiology: A case of HLH in the outpatient setting

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Hemaphagocytic lymphcytosis (HLH) is characterized by progressive histiocytic proliferation of non-malignant lymphocytes and macrophages. Excessive proliferation of these cells is the result of unchecked immune cell activation which leads to abnormal inflammation and tissue destruction. There is generally impaired regulatory activity of natural killer cells and cytotoxic lymphocytes leading to excessive activation of macrophages with abnormal cytokine release. The disease has both sporadic and familial presentations. Familial or primary HLH is a heritable disorder that is associated with 1 of 5 identified gene abnormalities, and symptoms usually present within the first few months of life. Sporadic or secondary HLH is often triggered by activation of the immune system during infections, autoimmune disorders, or other inflammatory states and can present at any age.

A 32 year old African American female presented to the outpatient adult medicine office of Wilmington Hospital complaining of 2 weeks of intermittent left leg and hand cramping with associated numbness. The symptoms were not triggered by any specific activities and were the latest symptoms in a presentation that included 3 months of persistent high grade fevers, chills, night sweats, fatigue, progressively worsening dyspnea on exertion, abdominal distention, poor appetite with associated nausea and vomiting, and a 25 pound weight loss. She was also concerned about worsening “yellowing of her eyes” over the last 2 months. Her physical exam was significant for scleral icterus, hepatomegaly and inguinal lymphadenopathy. She presented to the emergency room 2 months ago with similar symptoms and left neck swelling. At that point, imaging, including a PET scan, had demonstrated diffuse bulky lymphadenopathy and hepatosplenomegaly. Blood cultures were negative and viral assays ruled out HIV, CMV, EBV and hepatitis. She underwent a cervical lymph node biopsy and bone marrow biopsy that was consistent with lymphohistiocytic proliferation but negative for lymphoma. Repeat viral assays remained negative and she was subsequently referred to infectious disease for further workup. The diagnosis of HLH was made soon after.

HLH, though rare, should be strongly considered in presentations of diffuse lymphadenopathy and weight loss as demonstrated by this case. The presentation is similar to more frequently considered etiologies such as HIV and B-cell lymphomas, and as a result is often not considered until much later in the diagnostic work up. Delayed diagnosis significantly increases the risk of mortality as prompt induction of immunotherapy is essential for survival. Earlier consideration of this disease entity during the work up phase might facilitate prompter treatment and eliminate unnecessary repeat testing.
PENNSYLVANIA POSTER FINALIST - CLINICAL VIGNETTE Kenyetta Givans

PICC LINE CAN PICK THE HEART!

First Author: Kenyetta Givans, BA Dev Basu, MD Angela Wang, MD Vijay Rajput, MD, FACP

Background: Peripherally Inserted Central Catheters (PICC) are commonly used for prolonged intravenous access in acute care, home care and skilled nursing facilities. The incidence of new atrial arrhythmias from a central venous access device is up to 41% and 25% for ventricular arrhythmias. Clinically significant arrhythmias from PICC lines are not well described or reported in literature.

CASE: A 59 year old white male was transferred from an outside hospital with back pain, fever and neurological deficits and found to have an epidural abscess with MRSA positive blood cultures. Emergent debridement and drainage of abscess without complications was performed and a PICC line was inserted for long term antibiotics. A chest x-ray showed the tip at the cavo-atrial junction. On the night of insertion he had two episodes of asymptomatic runs of supraventricular tachycardia (SVT) lasting for several minutes. He had no history of arrhythmias and had been uneventful on telemetry while in the hospital. A chest x-ray was obtained to recheck the PICC line position which was unchanged. Nonetheless the PICC line was retracted by 2-3cm and repeat imaging showed it to be in the mid superior vena cava. After retracting the line there were no further episodes of SVT. We were not aware of our patient’s arm position during his runs of SVT.

Discussion: PICC lines have several risks and complications including infection, phlebitis, air embolism, thrombus formation, malposition of catheters, nerve injury, difficult removal and occasional breakage of catheters. Cardiac arrhythmias including SVT and ventricular tachycardia are rare complications of PICC lines based on our literature search. PICC lines are inserted by the well trained PICC teams or interventional radiologists and the position is routinely confirmed with a chest X-ray. The ideal position being two centimeters below the sternoclavicular joint but in cadaver studies PICC lines inserted via the basilic veins can move up to 2.8cm with changes in arm position. A few case reports showed inward movement of the tip of the PICC with adduction of the arm causing arrhythmias and resolution of arrhythmia with retraction of the line. Arrhythmogenic complications also include life threatening ventricular arrhythmias. These arrhythmias may be refractory to treatment due to the mechanical irritation caused by the catheter. Patients with newly developed or worsening arrhythmia must have the position of the PICC line evaluated and it should be considered as a possible etiology.

Summary: Patients with PICC lines who develop new or worsening arrhythmias require careful evaluation of the position of the catheter and relation with arm movements. Retraction of the PICC by a few centimeters can resolve the arrhythmia and decrease unnecessary costly cardiology evaluation and treatment.
Viral hepatitis complicated by hemolytic anemia and pneumonia in a traveler from India.

First Author: Sharon Li, Alejandro Delgado, Aaron Martin, Bryan Hess.

Introduction: Hepatitis A (HAV) and E (HEV) are common viral causes of hepatitis. The prevalence of infection is greatest in developing countries, but both viral infections are known to be distributed worldwide. Both infections are transmitted primarily through the fecal-oral route. Infection is often self-limited with complete recovery and no long term morbidity, conferring lifelong immunity, but on occasion, both can be causes of fatal acute liver failure. Extrahepatic manifestations of these diseases are rare but have been described in the literature.

Case: A 32 year old traveler from India presented to a local emergency room with malaise, nausea, vomiting and jaundice. He first felt ill on his flight from India to the United States. On physical examination, the patient appeared in mild distress and was diffusely jaundiced. Liver function tests drawn at the time of presentation demonstrated severe transaminase elevation with AST of 5897U/L, ALT of 6963U/L and total bilirubin greater than 50mg/dl. Serum Hepatitis A IgM antibody was reactive. The patient was hospitalized and treated with conservative management. Within 72 hours the patient demonstrated improving transaminases but developed severe hypoxemia concerning for multifocal pneumonia. He was transferred to our institution’s ICU where he was found to have a severe hemolytic anemia with a 5 gram drop in hemoglobin, LDH of 1100U/L and undetectable haptoglobin. A peripheral smear showed many reticulocytes with occasional target cells. Coomb’s testing was negative. He was treated with IV antibiotics for presumed HCAP and required blood transfusion. He recovered rapidly with a quick decline in oxygen needs and rapid resolution of hemolysis. Liver function tests normalized slowly but bilirubin remained higher than 30 through his hospital stay. Late during his hospitalization, the patient was found to have very low levels of G6PD activity as well as a positive hepatitis E IgM on repeat serologic testing.

Discussion: In endemic areas, coinfection of HAV and HEV is possible, but the rate is historically low, between 4.5-6%. A handful of case and institutional reports from regions endemic for hepatitis A have reported hemolytic anemia associated with hepatitis in patients with underlying red blood cell membrane defects or autoimmune disease. Additionally, lung complications of hepatitis A have been previously reported, particularly pleural effusions, but only in a few cases and predominantly in children. To our knowledge, lung damage has not been previously seen from hepatitis infection in adults. Here we present a man with hepatitis A and E infection that manifested so severely, it led to hemolytic anemia and acute respiratory distress.

This case serves as an example for potential atypical presentations and extrahepatic manifestations of a common disease, as well as concurrent hepatitis A and E infection. Vigilance is advised to avoid further morbidity/mortality.
An unusual case of spironolactone induced neutropenia

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Neutropenia, characterized by an isolated decrease in granulocytes with otherwise intact cell lines, is an alarming condition.

A 43 year old woman presented to the emergency department for evaluation of near syncope, fever, left upper quadrant abdominal pain, and malaise for the past week. Social history revealed that the patient works as a nurse and lives on a livestock farm. She had no significant past medical or surgical history, and was taking no medications, including over the counter or herbals. Prior to admission, she was seen by another practitioner for hirsutism and was prescribed spironolactone 50mg once daily. Six days prior to admission, she was seen by her family doctor for near syncope and instructed to stop the spironolactone. Physical exam noted no rash, hepatosplenomegaly, adenopathy, or thrush. She complained of tenderness to palpation in the left upper quadrant. CBC with differential revealed: a hemoglobin level of 13.2 g/dL, platelet count of 245,000, and an absolute neutrophil count (ANC) of 69. No other abnormalities were noted on her differential. Broad spectrum antibiotics were initiated with Cefepime and Vancomycin. Blood and urine cultures collected prior to antibiotics were negative. Further testing for viral and tick-borne illnesses was negative. Peripheral blood flow cytometry revealed a relative reactive lymphocytosis. On hospital day two, ANC was 38; on day three, her ANC had increased to 626; and on the day of discharge ANC was 1293. Ten days after presentation to the emergency department her ANC had returned to normal limits at 5375.

Spironolactone is a commonly used medication linked to neutropenia in patients with significant co-morbidities. Although there is limited literature on this phenomenon, most reports have been in patients with renal or liver dysfunction on diuretic therapy. However, this patient possessed no co-morbidities and the severity of the neutropenia was unusual.
Distal renal tubular acidosis and diabetes insipidus leading to the diagnosis of Sjogren syndrome

First Author: Jonathan W Yadlosky MS4 Other Authors: Elijah Grillo MS4, Loheetha Ragupathi MD, Ravi Sunderkrishnan MD Final Author: Seyed Hamrahian MD

Clinical Presentation: A 37 year old female presented with progressive fatigue over the course of three months, and debilitative weakness, nausea, and non-bloody non-bilious vomiting over the course of one week. Initial vital signs showed episodes of sinus bradycardia responsive to atropine, and were otherwise within normal limits. Physical examination showed profound bilateral upper and lower extremity weakness, without focal neurologic deficits. Laboratory studies on admission showed severe hypokalemia with potassium of 1.1 mEq/L, non-anion gap metabolic acidosis with pH 7.07 and bicarbonate of 9 mg/L, and renal insufficiency. Although the sodium level was normal at presentation, it increased to 159 mEq/L the following day. On the second day of admission, she developed hypoxemic respiratory failure, and was intubated and mechanically ventilated. Subsequent laboratory studies revealed positive urine anion gap, inappropriately high urine pH, elevated transtubular potassium gradient, persistent hypernatremia, along with a low urine osmolality and high serum osmolality. This combination of renal insufficiency, distal type renal tubular acidosis and diabetes insipidus prompted an immunologic work up for tubulointerstitial disease. High titers of anti-nuclear, anti-SSa and anti-SSb antibodies were found, suspicious for primary Sjögren's syndrome. A biopsy of the salivary glands of the lip showed focal lymphocytic sialadenitis, confirming the diagnosis of Sjögren's syndrome.

Discussion: Interstitial nephritis is a well described extraglandular complication of Sjögren's syndrome; the prevalence for renal tubular acidosis in particular ranges from 20-30% of Sjögren's syndrome cases. This case is unique in that the diagnosis of Sjögren's syndrome made solely on the basis of renal manifestations without any overt physical findings of the disease. There is no available data on the treatment of renal manifestations of Sjögren's disease, although many reports have suggested improvement with corticosteroids and immunosuppressants. This patient was treated with a course of corticosteroids, and with amiloride, following which her electrolyte abnormalities improved.
A Pain in the Neck: A Pott’s Disease Case Study

First Author: Caitlin Naureckas Second Author: Jonathan Movson, MD Third Author: E. Jane Carter, MD

TB infection of the spine (Pott’s disease) represents approximately half of all skeletal cases of TB but <1% of all TB cases. Due to rarity in developed countries, this diagnosis is often missed or delayed leading to poor outcomes. A 21-year-old male presented to the ED with severe neck pain progressing over six months without history of trauma. He noted night sweats with 20-pound weight loss; ROS was otherwise negative. Born in Guatemala, he had been in the U.S. for two years working as a dishwasher. He denied exposure to TB and history of TB screening.

On physical exam, vital signs were normal. Neurological exam was unremarkable. Tenderness to palpation was noted at the base of the neck with limited range of motion secondary to pain but no palpable swelling or mass. Chest radiograph showed clear lungs except for post-obstructive pneumonitis caused by central adenopathy. Cervical MRI demonstrated a rim enhancing mass, consistent with abscess, in the pre-vertebral space at the C2/3 level. An inflammatory process extended from C6 to the skull base. A separate inflammatory process was present on the left from C4-C7. The posterior mediastinum contained a small abscess adjacent to T3.

Patient was admitted to the hospital for ultrasound-guided biopsy of the posterior neck mass. Pathology demonstrated necrotizing granulomata, AFB smear negative. Fiberoptic bronchoscopy demonstrated no endobronchial pathology; washings were AFB smear-negative. PPD testing was positive (14 mm). Patient was started on isoniazid, rifampin, pyrazinamide, and ethambutol with aggressive pain management. He was discharged to the local TB clinic under directly observed treatment (DOT). Within two weeks Mycobacterium tuberculosis was cultured from his neck mass aspirate, sputa (expectorated), and bronchial washings. Drug susceptibility testing demonstrated pan-susceptibility, at which point ethambutol was discontinued. After two months his regimen was simplified to INH and rifampin 3x/week for ten months.

Surgical decompression with hardware stabilization of the cervical abscess was considered. Given his young age and lack of neurologic findings, it was elected to follow him closely with the intent to operate if neurological compromise appeared. Images obtained at the end of treatment demonstrated complete resolution. Indications for surgical intervention in Pott’s Disease include neurological sequelae, spinal instability, significant kyphosis, or refractory pain; the decision should not be based solely on imaging. Given the patient’s young age and lack of neurological symptoms, medical management with close follow-up was pursued instead of aggressive surgical correction. Rapid initiation of treatment coupled with aggressive pain management and close medical follow-up solved the problem of this pain in the neck without turning an acute problem into a chronic one.
S. gallolyticus endocarditis in a patient with a history of ulcerative colitis

First Author: Ravi Sarpatwari Lindsey Cilia, MD Manasa Ayyala, MD

**Introduction:** *Streptococcus gallolyticus,* formerly *Streptococcus bovis biotype I,* is a group D streptococcus that is known to cause infection in humans. In particular, *S. gallolyticus* endocarditis is significantly associated with concurrent colorectal cancer, although the mechanism of this association is much debated. Despite this frequent association, there are few case reports linking *S. gallolyticus* bacteremia with other conditions such as inflammatory bowel disease (IBD).

**Case Description:** 64 y/o woman presented to the emergency room due to urging of her primary care physician because of a drastic 30-lb weight loss over the previous four months. She had a history of ulcerative colitis (UC), hypertension, osteoporosis, and depression. Past medical history was notable for three negative colonoscopies within the past year. Since a previous hospitalization four months prior for acute back pain secondary to a fall, the patient complained of depressed mood and generalized weakness, self-imposing bedrest. Review of systems was significant for decreasing appetite without dysphagia or changes in abdominal symptoms from her baseline. The patient was also having episodes of lightheadedness and dyspnea on exertion but denied any fevers or chills.

Physical exam was significant for pale conjunctiva and a new III/VI holosystolic murmur at the left lower sternal border. Labs were notable for Hgb 8.7, MCV 72.4, and a negative FOBT. Given her past history of UC and marked weight loss, there was initial concern for a missed malignancy. With no known prior history of murmur, a transthoracic echocardiogram was obtained revealing a 12x15 mm mass on the posterior mitral valve leaflet suggestive of a vegetation as well as mitral regurgitation. Two sets of blood cultures taken on admission returned positive for *S. gallolyticus,* and patient was transitioned from empiric antibiotics to IV penicillin. A repeat colonoscopy revealed moderate inflammation from the rectum to the cecum that was unchanged from previous examinations. Multiple biopsies confirmed chronic inactive colitis, with the exception of one biopsy showing low-grade dysplasia. An MRI was obtained with concern for spondylodiscitis given bacteremia and history of compression fractures and was positive. Due to size of vegetation and worsening valvular function, a mitral valve replacement was performed, and the patient was discharged on long-term IV antibiotics.

**Discussion:** Although *S. gallolyticus* endocarditis is most commonly associated with colorectal cancer, infection by this organism should also be considered in patients with chronic gastrointestinal processes such as IBD. Given the symptoms of weight loss and weakness in the setting of UC, suspicion for malignancy remained high; however, the patient’s repeat colonoscopy revealed no evidence of colorectal cancer. In this case, inflammation caused by UC was suspected to promote translocation of gut flora leading to subacute endocarditis and the insidious onset of the patient’s symptoms. This case highlights the importance of a thorough history and physical exam, and that *S. gallolyticus* endocarditis can develop in patients without evidence of colorectal malignancy.
A Series of Unusual Lows: A Case of Non-islet Cell Tumor Hypoglycemia

Zoe Weiss MS3, Mary Angelynne Esquivel, MD, Harikrashna Bhatt, MD

Rare causes of hypoglycemia unrelated to anti-diabetic medications include neoplasias, auto-immune disorders, and insulinomas. Non-islet cell tumor hypoglycemia (NICTH) is an uncommon complication of various malignancies, specifically of mesenchymal or epithelial origin. We report a case of severe hypoglycemia in a patient with known metastatic hepatocellular carcinoma (HCC). A 54-year-old man with hemochromatosis, HCV cirrhosis and metastatic HCC s/p transcatheter arterial chemoembolization, was admitted for loss of consciousness in the setting of hypoglycemia (BG 15 mg/dL). He had stable vital signs and exam was notable for ascites and LE edema. Laboratory workup included a normal serum insulin 4.7mu/L (Nl: 3-25), low C-peptide 0.5ng/mL (Nl: 0.8-3.1), low IGF-1 23 ng/mL (Nl: 68-245 ng/mL), normal IGF-2 253 ng/mL (Nl: 47-350), absent serum ketones and normal baseline serum AM cortisol 5.6 ug/dL and post-ACTH stimulation cortisol levels of 23.1 and 25.9 (at 30 and 60 minutes, respectively). CT of the abdomen/pelvis showed a cirrhotic liver with multiple masses, splenomegaly, lung metastases, left portal vein thrombosis and non-specific calcifications in the right adrenal gland; no mention of pancreatic involvement. He received intravenous dextrose and high dose steroids, which improved his hypoglycemia. Attempts to wean him off the intravenous dextrose were unsuccessful.

About half of patients with NICTH present with hypoglycemia; symptoms include confusion, lethargy, diaphoresis, somnolence, and coma. Most patients appear ill with a large tumor burden. The most common pathophysiology is secretion of incompletely processed IGF-2, a hormone with biochemical homology to insulin. Although only 1/10 as potent as insulin, in high amounts it stimulates insulin receptors, suppresses glucagon, growth hormone release, glycogenolysis, and gluconeogenesis. Other described mechanisms include autoantibodies targeting insulin/insulin receptors or in some cases direct destruction of the liver and/or adrenal glands. The laboratory findings typical of NICTH include hypoglycemia, low serum insulin, low C-peptide, low beta-hydroxybutyrate, normal AM cortisol (if no adrenal insufficiency), and IGF-2:IGF-1 ratio >10. The prevalence of NICTH is unknown given its rarity and thus no clear standards of care are established. Described treatments focus on first correcting the hypoglycemia with glucagon, glucose, enteral or parental nutrition, then controlling the tumor source through resection, palliative debulking in nonresectable cases, chemotherapy, radiation or selective embolization. Optimal medical management includes glucocorticoids (which work by increasing IGF-2 clearance), long-term glucagon infusions, and recombinant human GH. Somatostatin and diazoxide have been used unsuccessfully.

This patient’s IGF-2:IGF-1 ratio of 11 along with his clinical response to high-dose steroids in the setting of normal adrenal function, was consistent with NICTH, likely due to an IGF-2 mediated paraneoplastic process. It is important to consider NICTH as a cause of severe, recurrent hypoglycemia in patients with known malignancy. Treatment with steroids is vital in restoring euglycemia and preventing complications from hypoglycemia.
Presentation and Diagnosis of Systemic AL Amyloidosis

Katie Anderson, BS, Tiffany O’Neill, DO, Ryan Weldon, MD, Livia Tsien, MD, Deborah DeWaay, MD, Medical University of South Carolina, Charleston, SC

Learning Objectives 1. To understand how amyloidosis can cause autonomic dysfunction 2. Learn how to diagnose amyloidosis

Case presentation: A 70 yo African-American female with a history of breast cancer and hyperlipidemia presented with weakness and syncopal events. Prior to presentation, she had a 6-month history of weakness with an associated 45lb weight loss. She also complained of a sandpaper-like feeling in her toes and a 2-week history of diarrhea. Physical examination was positive for severe orthostatic hypotension refractory to IV fluid replacement. A stress test, echocardiogram, colonoscopy, EGD, and PET scan were all negative. 24-hr urine collection showed heavy proteinuria (14g per day) and electrophoresis showed monoclonal IgG kappa and lambda levels at levels too low to quantitate. A fat pad biopsy with Congo red stain was negative for amyloid. Kidney and bone marrow biopsy both later confirmed lambda chain amyloidosis.

Discussion: Systemic AL amyloidosis results from the clonal expansion of plasma cells. The plasma cells secrete immunoglobulin light chains, which then deposit in the extracellular space around various organs. The presentation of systemic AL amyloidosis, therefore, can be variable and frequently begins with nonspecific symptoms. In our patient, the disease originally caused fatigue and weight loss but then rapidly progressed to involve the kidneys, peripheral nerves, and GI system. The involvement of the autonomic nervous system contributed to the severe orthostatic hypotension that our patient experienced.

The diagnosis of amyloidosis requires visualization of the amyloid fibrils via tissue biopsy. SPEP and UPEP are not useful screening tools because the light chains are not present in high enough qualities. While fat pad biopsy is less invasive, it has a lower sensitivity than a renal biopsy and may not provide definitive diagnosis.
TENNESSEE POSTER FINALIST - CLINICAL VIGNETTE Kristin Burkhalter

Case of an Unrelenting Runny Nose!

Kristin Burkhalter Nanette Bentley MD Mukta Panda MD FACP

Learning Objectives:

1.) Discuss methods available for diagnosing suspected cerebrospinal fluid leak.
2.) Discuss treatment options and long term outcomes.

Case: A 47 year-old female presented with two-day history of flu-like symptoms, high fever, and nonproductive cough. Review of systems positive for chronic headaches, sinusitis, rhinorrhea, and dizziness. History of childhood asthma with escalation in acute exacerbations and chronic sinusitis over 5-6 years. Smoked 1 pack/day for 30 years. Admission vitals normal. Significant exam findings included frontal and maxillary sinus tenderness; coarse breath sounds, diffuse inspiratory and expiratory wheezing bilaterally. Lab data showed normal CBC, BMP, negative influenza A/B nasal swab, CXR normal. Further history revealed an incident of domestic abuse and nasal fracture 6 years prior. She received systemic steroids, bronchodilators, and antibiotics for acute sinusitis/bronchitis. CT sinuses revealed acute on chronic sinusitis; communication between left frontal/ethmoid sinuses and intracranial cavity. MRI brain revealed soft tissue densities filling the left frontal, maxillary, and sphenoid sinuses. Dandy maneuver was negative. Suspicion for CSF leak was high, nasal secretions sent for ß-2 transferrin test confirmed presence of CSF rhinorrhea. Patient had left ethmoidectomy, nasal septoplasty, and cartilage grafting of posterior frontoethmoid sinus defect. Two years after surgery, she has had improvement in her sinusitis and overall asthma control.

Discussion: Trauma has been associated with approximately 90% of cases of CSF rhinorrhea, however this complicates only 2% of head traumas. The most common presentation of acute CSF leak is unilateral, chronic rhinorrhea, but can also present with symptoms of anosmia, vision and oculomotor impairments, meningitis. In the chronic phase, symptoms include headaches, recurrent meningitis, abnormal taste. Multiple detection methods are available once this diagnosis is suspected. Glucose content of suspicious fluid not recommended given the incidence of false negatives and positives. ß-trace protein has less false results but not specific to CSF. However, detection requires less time and technology. The test of choice for definitive diagnosis is detection by immunofixation of ß-2 transferrin; only produced in the CSF, aqueous humor, perilymph. Sensitivity and specificity is 99% and 97%. Once diagnosis made, imaging is necessary to locate the defect. The modality of choice is high resolution CT scan to identify bony defects. This can be followed with MRI to evaluate for soft tissue defects. While most CSF leaks resolve spontaneously within 1-2 weeks, some require intervention. Conservative management involves bed rest and avoidance of actions raising intracranial pressure. Use of prophylactic antibiotics to prevent meningitis is controversial. If leak does not resolve, endoscopic endonasal surgery preferred. Asthma and chronic sinusitis are commonly seen by internists, this case highlights the importance of keeping CSF rhinorrhea in the differential when these conditions are not resolved or progress despite conventional management.
Texas Poster Finalist - Clinical Vignette Sara Cromer

To Clot or Not to Clot: Lupus Anticoagulant-Hypoprothrombinemia Syndrome Treated with Rituximab

First Author: Sara Cromer, Baylor College of Medicine Second Author: Natalie Uy, Baylor College of Medicine Last Author: Courtney Miller-Chism, MD, Baylor College of Medicine

While lupus anticoagulant (LA) is classically associated with venous and arterial thromboses, bleeding episodes with positive LA serum studies suggest an antibody to prothrombin. We contribute a case in which bleeding was refractory to gratuitous administration of fresh frozen plasma (FFP) but resolved after administration of corticosteroids and rituximab.

A 57-year-old Hispanic male with history of alcohol abuse presented with gross hematuria preceded by flank pain and non-traumatic epistaxis for 3 days. He denied prior bleeding episodes, family history of hematologic or auto-immune disorders, and usage of antiplatelet or anticoagulant medications. On presentation, vital signs and physical exam were within normal limits, with the exception of mucosal bleeding and petechiae on the soft palate. Labs were remarkable for slight leukocytosis (12,100/µL), significant elevations in prothrombin time (PT, 33.6s) and partial thromboplastin time (PTT, 130.6s) with an INR of 3.6, and gross hematuria. Liver profile, D-dimer, and fibrinogen were normal. A mixing study showed correction of PT but incomplete correction of PTT. After a precipitous drop in hemoglobin to 5.5 mg/dL (from 15.4 mg/dL on admission), up-trending INR to 4.5, and development of mild headaches, abdominal and head CT scans on hospital days (HD) 2 and 3 showed spontaneous and progressing retroperitoneal hemorrhage and interval development of two small subdural hematomas. He was admitted to the intensive care unit on HD 3 and started on 100 mg prednisone daily and vitamin K. Prothrombin complex concentrate, complex factor IX, and 36u of FFP were administered over three days with limited and fleeting clinical and laboratory improvement. On HD 4, he was found to have Factor II activity at 17% (normal 75-130%), and a positive LA. Bleeding continued until HD 6, and the decision was made to start weekly rituximab at 375 mg/m². His hemoglobin and INR stabilized that day, and he received only two units of FFP during the remainder of his hospitalization. Repeat factor II activity on HD 8 improved to 60%. He was discharged in stable condition on HD 13 with plan for a prednisone taper and a total of 4 cycles of rituximab which were completed without complication as an outpatient. Coagulation studies remained stable two months after discharge.

Lupus anticoagulant-hypoprothrombinemia syndrome (LAHS) should be suspected when patients with positive LA present with a bleeding diathesis. In this syndrome, non-neutralizing anti-prothrombin antibodies lead to increased clearance of prothrombin and diagnostic studies suggesting both an inhibitor and a factor deficiency. LAHS is treated with factor replacement (FFP), but several case reports suggest that immunosuppressants may play an important role in treatment. Corticosteroids raise prothrombin levels by decreasing clearance of prothrombin-antibody complexes but do not prevent new antibody production. In this case, rituximab infusion normalized the patient’s INR and prevented progression of developing retroperitoneal and subdural hemorrhages, supporting its clinical utility in the treatment of LAHS.
Castleman’s Disease: An Uncommon Cause of Chronic Anemia

First Author: Anna Garza, MSII University of Texas Medical Branch

Introduction: Chronic anemia in young women is often attributed to iron deficiency caused by heavy menstrual cycles or small bowel absorption deficiency. Less common causes can remain undiagnosed for years.

Case Presentation: A 25-year-old woman presented with a 13-year history of chronic anemia. The patient’s history was significant for heavy menstrual cycles as a teenager, however currently her cycles were normal. She had attempted various oral supplements throughout the years with no improvement in her hemoglobin. There was no family history of thalassemia or anemia. Physical exam was remarkable only for hepatomegaly and an ill-defined fullness in the left upper abdomen. Presenting laboratory studies: hemoglobin 7.7g/dL, MCV 61.6FL, platelets 569,000uL; metabolic panel revealed only an elevated alkaline phosphatase (709 IU/L). Iron studies: serum iron 24ug/dL, ferritin 49ng/mL, TIBC 256ug/dL, transferrin percent saturation 9%. Immunoelectrophoresis: IgG 3300mg/dL, IgA 400mg/dL, IgM 409mg/dL

Management included a trial of IV iron transfusions. Hemoglobin initially increased by 2 grams, then plateaued. Additional testing included an abdominal MRI, due to concerns of biliary disease, and a bone marrow biopsy. The MRI revealed hepatomegaly, measuring 24cm, with no ductal obstruction and a 5.9x6.9cm mesenteric mass with arterial enhancement. Bone marrow biopsy revealed no abnormalities. A liver biopsy showed sinusoidal dilatation most prominent in zone 1 and 2, with focal macrovesicular steatosis in less than 5% liver parenchyma, and mild perisinusoidal fibrosis with no portal inflammation. Biopsy of the mesenteric mass proved inconclusive showing about 95% lymphocytes with approximately equal B and T cells. The mass was removed by laparotomy; further pathology studies revealed Castleman’s lymph node of plasma cell variant.

Discussion: Castleman’s Disease (CD) is a heterogenous group of lymphoproliferative disorders in which lymph nodes become enlarged and swollen. Castleman’s can be subdivided into two distinct types: multicentric CD, with involvement of multiple lymph nodes, and unicentric CD (UCD) affecting a single node. Castleman's Disease is often associated with systemic manifestations and laboratory abnormalities including anemia, thrombocytopenia or thrombocytosis, hypoalbuminemia, polyclonal hypergammaglobulinemia, elevated IL-6 and others. Abnormalities often resolve with resection of the enlarged node in UCD. The pathogenesis of this disease is poorly understood. An exaggerated response of the immune system, often to normal stimuli, is thought to play a role in initiation of the disease. The specific cell within the lymph nodes to induce this reaction is not known. Studies have linked IL-6 overproduction to systemic manifestations. The histological changes are similar to those often seen in autoimmune disease. Because patients are frequently asymptomatic, discovery of Castleman’s often occurs incidentally. Prognosis following resection in UCD is excellent. The diagnosis of Castleman’s Disease may have remained a mystery, had it not been for this patient’s insistence on aggressive evaluation of her anemia.
A Classic Disease Often Forgotten in Modern America

Andrea Gaspar, Ahmed Salahudeen M.D., Giovanni Davogustto M.D., Jonathan Smith M.D.

Lead toxicity had become commonplace after the Industrial Revolution secondary to increased occupational and environmental exposure. Fortunately, awareness and regulation since the 1970’s has vastly diminished lead exposure, making its toxicity a rarity. The following case emphasizes the importance of lead toxicity as a differential diagnosis in a patient with vague abdominal pain.

A 42-year-old woman presented to the emergency department with several months of diffuse abdominal pain, characterized as an intermittent “biting” sensation that had worsened over the past three days. She also experienced nausea, vomiting, and proximal lower extremity cramping. On physical exam, she was in moderate distress due to pain and had minimal cognitive impairment. Abdominal exam was notable for diffuse tenderness to palpation. Laboratory data was remarkable for microcytic anemia, with a hemoglobin of 8.4 gr/dl and an MCV of 72 fl/cell. Her chemistries revealed hypophosphatemia, hyponatremia, and hypokalemia. Abdominal Computed Tomography and transvaginal ultrasound were unremarkable. Peripheral blood smear revealed basophilic stippling. Protoporphyrin level was elevated at 286 µg/dL. The constellation of symptoms and laboratory findings suggested the diagnosis of chronic lead toxicity, which was confirmed with a blood-lead level > 65 µg/dL. Treatment consisted of aggressive electrolyte replacement and lead chelation with oral succimer. Within five days, abdominal pain, cognitive disturbances, and electrolyte abnormalities had resolved. Succimer was continued after discharge, for a total of fourteen days. Her house – a 1920s building – was identified as the lead source, and she moved to a new home. Upon follow up three months later, her lead levels had significantly decreased to 32.5 µg/dL, and she remained asymptomatic.

The prevalence of elevated lead levels in adults is only 6.4/100,000, a number that has decreased by fifty-four percent over the last eighteen years. Ninety-one percent of lead exposures are occupational. Although elevated lead levels are never considered safe, the classic symptoms of chronic lead toxicity appear between 30-70 µg/dL. The ionic properties of lead disrupt the normal physiology of numerous biological processes. This results in a disparate clinical presentation that can include abdominal colic, anemia, muscle cramps, constipation, peripheral neuropathy, nephrotoxicity, and cognitive disturbances. Coupled with lead toxicity’s low incidence, these vague features make it a challenging diagnosis for modern clinicians. Treatment with chelation therapy can dramatically diminish these symptoms, and removal from the source of exposure can result in a permanent cure. Considering lead toxicity in patients with abdominal pain coupled with microcytic anemia and electrolyte derangements can minimize excessive testing and delays in therapy.
TEXAS POSTER FINALIST - CLINICAL VIGNETTE Skyler M White

Persistent leg infection due to Mycobacterium immunogenum

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Introduction: Cutaneous infections caused by nontuberculous mycobacteria (NTM) are increasing. Mycobacterium immunogenum is a new species of NTM associated with skin lesions. Historically, the majority of infections of NTM were attributed to contamination of municipal water systems due to inadequate equipment sterilization, because these organisms display resistance to standard disinfectants.

Case Report: A 30-year-old woman presented to the clinic for evaluation of a tender right leg lesion. She first noticed the lesion 2 months earlier during a vacation in Hawaii. During her travel she swam in pool and ocean water. She denied local trauma and had no pruritus, drainage, or bleeding. She was initially diagnosed with a staph abscess but had no improvement after a 3-day course of Augmentin. On exam, the patient had a violaceous, indurated nodule on the right anterior leg with ill-defined borders, overlying fine white scale and surrounding erythema. Augmentin was discontinued and the patient was initiated on twice daily doxycycline for 10 days with biweekly dilute bleach baths. Twenty-four hours later, the lesion developed drainage with a necrotic base after a wound culture. She was continued on doxycycline and started on mupirocin 2% ointment. The culture revealed infection with the rapidly growing mycobacterium species, Mycobacterium immunogenum, with susceptibility to amikacin and clarithromycin. Her therapy was changed to twice daily clarithromycin and warm compresses. The lesion showed improvement over the next two weeks with reduced erythema and size. After 8 weeks of treatment, the patient’s symptoms had fully resolved.

Discussion: M immunogenum was first characterized in 2001 as belonging to the Mycobacterium chelonae-Mycobacterium abscessus group of NTM. It is a rapidly growing aerobic Gram-positive, acid- and alcohol-fast, non-pigmented bacillus. Identification of new NTM species has been possible due to genetic methods of identifying the 16S rDNA sequencing. Also, PRA patterns of the hsp65 gene make M. immunogenum identifiable.

M immunogenum was initially named for its association with hypersensitive pneumonitis in metal factory workings, but it has also been implicated as the causative agent in several reported skin infections following penetrating trauma, tattoos, and catheter-related infections. M. immunogenum demonstrates resistance to a variety of disinfectants, biocides, and has the ability to form biofilms. Immunocompromised hosts are especially at risk to disseminated infections, which present...
with multiple painful skin nodules or draining abscesses.

Reported cases of skin infections are limited, with the first case of an immunocompetent patient published in 2005. The best treatment for cutaneous *M. immunogenenum* infections is still not known. Tissue culture with species identification should be performed on persistent skin lesions to determine appropriate treatment as this NTM displays multi-drug resistance.

**Reference**

US AIR FORCE POSTER FINALIST - CLINICAL VIGNETTE 2LT Amy Jiang

CONGENITAL CD4 DEFICIENCY WITH MAC-RELATED CHYLOUS ASCITES

First Author: Amy Jiang Second Author: Eric Zhao, MD

Disseminated *Mycobacterium avium* complex (MAC) infection usually presents as a rare complication of advanced HIV infection usually occurring in patients with CD4 counts <50 cells/µl. Chylous ascites is a known, but also relatively rare complication of MAC infection. Here we report a case of congenital CD4 deficiency with MAC-related chylous ascites.

A 34 year old male presented to Tampa Regional Hospital with increasing abdominal pain and bloating, back pain, generalized fatigue, and weight loss of 100lbs over the course of one year. His past history is relevant for a skin infection at age 6 that was acquired after swimming in a lake. It is unclear what biopsies and cultures showed at that time, however he was treated with rifampin, erythromycin, ethambutol with resolution of infection. He did well until he was 32 (2012) when he began developed “burning” lung pain after working as a lineman in Louisiana. He did not seek medical attention at that time. On physical exam during current presentation, patient was noted to be cachectic with temporal wasting and a markedly distended abdomen with dullness on percussion. CT abdomen showed mesenteric retroperitoneal lymphadenopathy and bilateral adrenal masses. He underwent paracentesis, and peritoneal fluid analysis showed SAAG >1.1, high triglyceride content, and 75 leukocytes/µl. Adrenal biopsy was positive for AFB. Patient was placed on rifampin, moxifloxacin, ethambutol, and azithromycin, however, he continued to accumulate chylous ascites requiring frequent paracentesis in the following months. Decision was made to perform transjugular intrahepatic portosystemic shunt (TIPS) or further treatment of the refractory ascites. The procedure was complicated by continuous clotting of the shunt requiring heparin infusion. Patient was placed on anti-coagulation and did well post-procedure.

This case highlights some of the difficulties in treatment for people with CD4 deficiency and liver failure due to disseminated MAC infection.
GRAM-NEGATIVE SPINAL INVADERS

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Background: Orthopedic surgery site infections (SSI) previously were demonstrated to be frequently gram positive with few incidence of gram-negatives (1-3). The current focus for prophylaxis typically uses gram-positive perioperative antibiotic coverage. Here, we present two recent cases of routine surgeries complicated with a gram-negative SSI.

Case Presentation: The first case is of a 68 year old African American male who underwent a L3-L4, L4-L5 decompression, with arthrodesis, grafting, and hardware placement. The patient received Cefazolin for infection prophylaxis. He tolerated the procedure well with no complications and experienced an uneventful postoperative hospital course. One week after discharge, the patient returned with 3 days of fever, lower back pain and right anterolateral thigh pain. MRI of his spine showed a large fluid collection posteriorly at the site of the hardware extending superficially into the subcutaneous tissue, suggestive of post-operative wound abscess. Cultures of this fluid grew Proteus mirabilis susceptible to Moxifloxacin. He was transitioned to Moxifloxacin and clinically improved.

Patient DG, a 47 year old female, underwent a L4-L5 right-side laminotomy, foraminotomy, and excision of the intervertebral disk for a L4-L5 disk herniation after falling from a horse. Clindamycin was used for infection prophylaxis due to her Penicillin allergy. Several days later she underwent a surgical revision with Clindamycin prophylaxis for continued pain thought to be from a recurrent disk fragment. 10 days after initial surgery she presented with fever (38.9 C) and back pain. This progressed to include an osteomyelitis/diskitis of the surgical site. Blood culture and operative tissue culture both grew Serratia susceptible to Ciprofloxacin. The patient was treated with Ciprofloxacin and improved clinically.

Discussion: The importance of infection prevention cannot be overstated. In the case of our two patients, one underwent multiple surgical revisions and the other required additional hospitalization. A retrospective analysis of 239 cases of SSI in spine surgery unexpectedly identified that gram-negatives accounted for 30.5% of the cases of which a majority were Cefazolin resistant (4). This same study also noted the number of infections due to gram-negative bacteria increased with distal surgical level. Antibiograms at individual hospitals should offer insight into hospital specific antibiotic prophylaxis based on bacterial resistance rates. Also, study into infection rates at the hospital specific to surgical site and for the hospital in general would offer additional clues for antibiotic prophylaxis.

References
WASHINGTON POSTER FINALIST - CLINICAL VIGNETTE Roderick Yang

A rare reaction disguised as sepsis

First Author: Roderick Yang Second Author: Karthik Ragunathan, MD Third Author: Kavitha Kalvakuri, MD

OBJECTIVE: Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a rare, potentially life-threatening drug-induced hypersensitivity reaction typically associated with anti-epileptic agents (e.g., phenytoin, carbamazepine, lamotrigine). We present an unusual case of DRESS syndrome secondary to trimethoprim-sulfamethoxazole.

CASE REPORT: A 30 year old African American woman presented to the emergency department with a one week history of fever, chills, sore throat, vomiting, diarrhea, and light headedness. She denied joint pains, headache, blurred vision, and dysuria. She was scheduled for elective right nephrectomy in one week for recurrent pyelonephritis and was on prophylactic trimethoprim-sulfamethoxazole, initiated 17 days prior to presentation. Physical exam was significant for a blanching rash on the face. Significant labs included a leukocyte count of 2,700 cells per microliter with 7% eosinophils, creatinine of 1.24 milligrams per deciliter (mg/dL), procalcitonin level of 4.6 nanograms per milliliter, and a C-reactive protein level of 8.46 mg/dL. Liver transaminases were within normal limits on admission but increased over the next three days to over 300 international units per liter (IU/L), while alkaline phosphatase reached 199 IU/L. Initial differential diagnoses included drug allergy, viral fever, and autoimmune conditions. On hospital day three, the patient developed severe acute respiratory distress, requiring intubation and transfer to the intensive care unit. Trimethoprim-sulfamethoxazole was discontinued in favor of empiric broad-spectrum coverage for suspected aspiration pneumonia, including vancomycin, piperacillin-tazobactam, and doxycycline. Despite her septic picture, cerebral spinal fluid studies, pan cultures, and all microbiological tests were negative. Anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, and anti-double stranded DNA testing did not reveal any abnormality. Abdominal computed tomography was unchanged from prior records. The patient continued to develop recurrent high-grade fevers up to 40C despite no evidence of bacteremia, leading to strong suspicion of an adverse drug reaction. Antibiotics were discontinued and the patient was given a short course of corticosteroids, which resulted in significant clinical improvement. She was discharged home on hospital day 13.

DISCUSSION: Rash, fever, eosinophilia, and transaminasemia two weeks after initiation of trimethoprim-sulfamethoxazole make DRESS syndrome the most likely etiology. This uncommon drug reaction typically develops two to four weeks after initiation of the offending drug. In contrast, Steven Johnson syndrome and toxic epidermal necrolysis typically present within two weeks. DRESS syndrome commonly involves the liver but can have multi-organ involvement. DRESS syndrome secondary to trimethoprim-sulfamethoxazole has rarely been reported. A high index of suspicion is required to diagnose the condition. Potential complications include prolonged hospitalization, multi-organ failure, and death. Clinical recovery typically occurs in six to nine weeks, but may be complicated by remissions and relapses. Aside from removal of offending drug, treatment is primarily supportive. Corticosteroids are often used in severe cases, though data to demonstrate their efficacy in DRESS syndrome are lacking.
TB or Not TB: Mycobacterium genavense as a Cause of IRIS in a Patient with HIV Infection

First Author: Dorothy Knutsen Other Authors: Nicole Bryan, MD, PhD, Nasira Roidad, MD, Melanie Fisher, MD, MSc, FACP

Introduction Nontuberculous mycobacteria (NTMB), such as Mycobacterium avium complex, are well known to cause disseminated infections in immunocompromised patients, including those with HIV infection. These infections often go unrecognized in patients with advanced HIV disease, until antiretroviral therapy is started and the immune system is reactivated. This process is known as immune reconstitution inflammatory syndrome (IRIS). Here we present a case of a patient with necrotizing lymphadenitis caused by a rare species of NTMB that was initially mistaken for tuberculosis.

Case Description This patient is a 34 year old Mexican immigrant who was diagnosed with HIV in September 2013. He was soon started on antiretroviral therapy with a subsequent rise in his absolute CD4 count from 68 cells/µL (8%) to 245 cells/µL (14%). Approximately 6 months after starting therapy, he developed a small lump on the right side of his neck that evolved into a large, painful neck mass. CT scans of his neck and chest showed multiple necrotic lymph nodes and a 6 mm pulmonary nodule in the left lung base. A fine needle aspiration of the neck mass was performed and the sample was found to have multiple acid-fast organisms present. However, the direct PCR probe for tuberculosis and the culture were negative. Given his numerous risk factors, the clinical suspicion for tuberculosis remained high and anti-tuberculosis therapy was initiated. In subsequent follow-up, the mass worsened despite treatment compliance. The original sample was sent for ribosomal RNA sequencing for definitive organism identification. The causative organism was identified as Mycobacterium genavense and therapy was adjusted to rifampin, azithromycin, and ciprofloxacin, based on current IDSA recommendations. After two weeks, the patient reported mild improvement in symptoms and a decrease in size of the mass.

Discussion Mycobacterium genavense is a ubiquitous form of NTMB that is known to colonize soil, birds, and the human GI tract. In immunocompromised patients it can cause a disseminated infection with diarrhea, fever, and abdominal pain. When HIV positive patients develop lymphadenitis, tuberculosis is at the top of the differential, particularly for those who have been to endemic areas. As symptoms often mimic tuberculosis, it is important to distinguish M. genavense from its well-known cousin as treatment differs significantly, and does not pose a risk of transmission to others. Diagnosis can prove to be difficult because M. genavense requires an extensive culture incubation period or identification through molecular techniques.

Conclusion Nontuberculous mycobacteria should be considered as a possible etiology in HIV positive patients who present with IRIS. Further organism identification is needed particularly if acid-fast stains are positive and tuberculosis cultures and PCR are negative as in this patient’s case.
A Rare Cause of Severe Transaminitis

First Author: Megan P Arnett, Medical Student, Medical College of Wisconsin, Milwaukee, WI

Introduction: Cocaine induced hepatic necrosis is a rare but potentially serious sequel of cocaine use. A rapid rise in transaminases after cocaine use, coupled with the absence of other possible causes of liver injury, should raise clinical suspicion of hepatic necrosis. While often self-limited with supportive care, patients with liver failure should be monitored carefully for more serious complications.

Case: A 44 y/o female with a PMH of bipolar disorder, GERD, and psychosis was brought to the hospital by EMS for mental status changes and likely substance ingestion. Per EMS report, she was a known sex-worker and was found confused in her hotel room with marijuana, pills, and a crack pipe. She had no hypoxia or hypotension. She received narcan for her respiratory depression, and was subsequently restrained in the ED for agitation. Labs revealed an anion-gap metabolic acidosis, mild AKI, CPK elevation to 7514 IU/L, and mildly elevated liver enzymes (ALT 76, AST 104 IU/L). Urine toxicology screen was positive for opioids and cocaine. While her CPK and creatinine improved with aggressive IVF resuscitation, her AST/ALT levels reached 5383/3425 by hospital day 3. Physical exam revealed mild RUQ tenderness, and her INR was elevated at 2.4, raising concern for hepatic failure. She did not develop encephalopathy, overt bleeding, or progressive renal insufficiency. A RUQ ultrasound did not show thrombosis and a viral hepatitis panel, HIV test, and acetaminophen level were negative. With continuous supportive therapy, the patient’s liver enzymes trended down and her INR normalized. She was discharged to in-hospital rehab on day 10, with AST/ALT of 282/1369. Two-week follow-up revealed enzymes nearly back to baseline.

Discussion: In this patient, common causes of severe transaminitis in the thousands were ruled out with a negative screen for viral hepatitis, absence of acetaminophen and salicylates on drug screen, a negative HIV test, a RUQ ultrasound and no documented episodes of hypotension. We hypothesized that this patient had transient elevation of liver enzymes secondary to acute hepatic necrosis caused by cocaine intoxication, a rare cause of transaminitis described in a few cases in the literature. This cocaine-mediated toxic effect is thought to be due to the minor pathway of cocaine metabolism in the liver that depletes NADPH/glutathione levels and forms toxic free radicals. Should a biopsy be performed, it most often shows necrosis in zone 3 of the liver, which corresponds to the distribution of cytochrome P-450. Rapid recovery is typical after withdrawal of the agent and supportive therapy, but patients should be monitored closely as cocaine-induced liver damage is often associated with multi-system dysfunction, including kidney failure, myocardial infarction and pulmonary edema. In severe cases, fulminant hepatic failure and even death can occur.
WISCONSIN POSTER FINALIST - CLINICAL VIGNETTE David Ritchie

DRESS Syndrome, a Rare Side Effect of Rifampin

First Author: David Ritchie Second Author: Dr. Saqib Baig

Introduction Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare and potentially fatal drug-induced hypersensitivity reaction that typically presents with fevers, skin rashes, internal organ inflammation, and hematologic abnormalities. The infrequency with which it is encountered in daily clinical practice makes diagnosing this syndrome a challenge.

Case A 54 year old Caucasian woman with a history of hypothyroidism and multiple orthopedic surgeries on her right femur presented with a 3 day history of fevers, chills and rash. One month prior to this visit, the patient was diagnosed with osteomyelitis after she underwent a washout and debridement of her right femur hardware and discharged home on Vancomycin and Rifampin. She had been doing well on the antibiotics for four weeks until the fevers and chills began. On presentation to the ED, she was hypotensive, febrile, and tachycardic with a diffuse, faint lenticular and blanching rash. After workup, the patient was diagnosed with a hypersensitivity reaction to Vancomycin. Her clinical symptoms improved on antibiotic holiday and she was discharged home on Daptomycin and Rifampin for treatment of her osteomyelitis.

One week later, the patient again presented to the ED with a new onset morbilliform rash and fevers. On physical exam she was hypotensive (80/50), tachycardic and febrile (103.7°F). Her skin exam was significant for a diffuse rash characterized by pink macules and papules that were worse on her upper extremities and upper back. There was no purpura, vesicles, pustules, or mucosal sloughing of the eyes or mouth. Symmetrical facial swelling and blepharedema were present. Labs revealed elevated liver enzymes (ALT/AST: 95/47U/L), increased alk phosphatase (378U/L), and elevated GGT (306U/L). Her CBC with diff on hospital day 1 was: WBC 9.3 with 5% eosinophils (absolute count 1000/UL). Given these findings and results from the RegiSCAR inclusion criteria, we diagnosed this patient with DRESS syndrome secondary to Rifampin. All antibiotics were discontinued and high dose prednisone was initiated. By hospital day 9, her rash and facial swelling had subsided. She was started on Linezolid to finish treatment for osteomyelitis and discharged home in stable condition.

Discussion DRESS syndrome can cause multisystem organ failure leading to a mortality rate of 10-20%. As of 2011, a total of 44 drugs have been implicated as the cause of DRESS syndrome. However, our literature search has revealed only 1 case report of rifampin induced DRESS syndrome. Treatment involves prompt recognition of the disease, removal of the offending agent, high dose steroids and supportive therapy.
WISCONSIN POSTER FINALIST - CLINICAL VIGNETTE Brian Michael Schultz

THORACIC AORTIC ANEURYSM 30 YEARS AFTER AORTIC VALVE REPLACEMENT

First Author: Brian Michael Schultz Second Author: James Sebastian, MD MACP

Introduction: Aneurysms of the proximal thoracic aorta (TAA) are increasingly recognized and often diagnosed on imaging studies performed for other indications. Proximal TAA has been frequently associated with a bicuspid aortic valve (BAV), one of the most common congenital heart anomalies diagnosed in adult patients. Some patients with BAV demonstrate progressive dilation of the proximal ascending aorta even after elective aortic valve replacement (AVR). This observation suggests that the pathophysiology of BAV “aortopathy” is likely multi-factorial and not strictly limited to increased wall stress due to abnormal flow characteristics across the aortic valve.

Case: A 54 year old man received regular follow-up in the Anticoagulation Clinic at the Milwaukee VAMC in order to monitor his chronic warfarin therapy following placement of a 27 mm Bjork Shiley aortic valve prosthesis in 1976 for aortic insufficiency that was attributed to a BAV. When the patient began to notice increased dyspnea on exertion and generalized fatigue in the fall of 2006, a transthoracic echocardiogram (TTE) was ordered to evaluate his left ventricular (LV) function. The TTE showed normal prosthetic valve function, mildly decreased LV ejection fraction but severe dilation of the aortic root. CT angiography demonstrated a fusiform aneurysm of the ascending aorta measuring 7.3 cm in AP dimension – the aortic arch, great vessels and descending aorta were all normal in caliber. The patient subsequently underwent aortic root replacement in February 2007 using a St. Jude 27 mm composite graft – his continued follow-up in the outpatient internal medicine clinic has been uneventful.

Discussion: Aneurysms of the proximal thoracic aorta have multiple potential etiologies including genetic syndromes (Marfan and Ehlers-Danlos), vasculitis/inflammatory diseases (Takayasu and Giant Cell Arteritis) and degenerative disorders. Clinicians should be aware that BAV has also been strongly linked to the development of proximal TAA. The aortic dilatation associated with BAV tends to occur more frequently and at a younger age than in patients with tri-leaflet aortic valves. BAV patients with isolated aortic insufficiency may be at increased risk of late aortic events compared with BAV stenosis patients even after the aortic valve has been replaced. Further studies are needed not only to ascertain the detailed pathophysiology but also to clinically determine the optimal timing and method of assessing the ascending aorta in BAV patients, including those patients who have previously undergone AVR.
CALIFORNIA PODIUM PRESENTATION - RESEARCH Jules Vieaux

Quality Improvement for Advance Care Planning Completion Rates in a Community Clinic

First Author: Jules Vieaux John MacMillan, MD Raminder Gill, MD Benjamin Mansalis, MD

Introduction: There is substantial evidence that the medical treatment people would choose at the end of life is commonly different from the treatment they receive. Individuals’ preferences for where they wish to spend the end of their lives are also often not met. It is generally agreed that Advance Care Planning (ACP) and Advance Directives (AD) are useful tools to provide the mechanisms for ensuring individual autonomy at the end of life. In fact, the National Committee for Quality Assurance evaluates medical records for Patient-Centered Medical Homes to determine that patients either have an ACP offered or documented. Nevertheless, fewer than 1/3 of American adults have an AD. Many studies have elucidated factors associated with increased completion of ACP and barriers to completion, but few studies have examined how the healthcare system can increase completion rates. Lifelong Over Sixty Health Center (OSHC) is Federally Qualified Health Center community clinic serving over 3000 geriatric patients from diverse socioeconomic backgrounds. Audits indicate the completion rate for ADs at OSHC is between 3-7%. A two-phase quality improvement pilot program was developed to determine the ideal workflow for increasing the rates ACP and ADs are offered to and completed by patients at OSHC.

Methods: During the first phase of the pilot program, we interviewed medical providers and staff to identify existing best practices and new strategies to improve the ACP process. The workflow was evaluated by scheduling and leading discussions with nine patients resulting in three completed ADs. The second phase investigated quality improvement strategies to increase ACP completion rates. We evaluated multiple referral strategies while developing and refining a discussion script to introduce ADs to patients. We deployed provider and patient surveys to understand motivations and barriers to ACP. Finally, we developed an EMR documentation strategy to facilitate accurate tracking of results.

Results: Over nine weeks, 99 patients were introduced to ACP services and given a copy of an AD during a 3-5 minute discussion while in clinic for other appointments. Each patient was offered the option of a future follow-up discussion either in-person, over the phone, or in a group meeting. 32 patients requested additional information, with 20 completing in-person discussions reviewing an AD, 10 completing a discussion over the phone, and 7 completing ADs. EMR documentation noted a 1.8% increase in the offering of ACP services across the clinic.

Conclusion: Initial research findings informed recommendations for improved ACP services with validated discussion scripts, a refined clinic workflow and clinic staffing recommendations. Future plans include program expansion to additional clinic sites and regular performance tracking.
Immunotherapy in Stage III melanoma: A population-based analysis of demographic and health system factors using National Cancer Database (NCDB)

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Introduction: Adjuvant systemic immunotherapy is currently the only approved treatment option for stage III melanoma. Its benefit in relapse-free survival and to a lesser extent overall survival is demonstrated in several randomized controlled trials and meta-analyses. The individual characteristics guiding a patient’s decision to undergo treatment, however, are yet to be elucidated. In this study we identify factors associated with immunotherapy use for treatment of patients with stage III melanoma.

Methods: This is a retrospective study of patients diagnosed with stage III melanoma between 2000 and 2011 (n=38287) from the NCDB. NCDB is a nationwide oncology outcomes database containing ~70% of newly diagnosed cases in the U.S from more than 1,500 accredited cancer programs in the United States and Puerto Rico. Chi-square analysis was used as the test of significance.

Results: On average, 24% of patients with stage III melanoma received systemic immunotherapy between 2000 and 2011. Immunotherapy use is significantly lower in African Americans (15% vs 24% in Whites), males (23% vs 25% in females), Medicare patients (10% vs 32% in privately insured), patients with household income < $28,000 (21% vs 24% in patients with household income > $33,000), those with multiple comorbidities (11% vs 25% in patients with zero comorbidities), or age >60 (13% vs 38% for ages <59). P-value for all comparison <0.01.

Conclusions: This is the largest epidemiologic study evaluating treatment patterns in patients with stage III melanoma. While adjuvant immunotherapy is the only available treatment option for stage III melanoma, it is not widely utilized. Factors associated with a decreased likelihood of receiving immunotherapy are male sex, black race, older age, Medicare coverage, lower household income, and multiple comorbidities.
Use of Signals and Systems Engineering to Improve the Safety of Warfarin Initiation


Introduction: Spurious laboratory values and post-analytical errors can lead to erroneous dosing of medications such as warfarin, a drug with a narrow therapeutic index. A spuriously low International Normalized Ratio (INR) value leading to warfarin overdose can create the potential for catastrophic hemorrhage. Sophisticated warfarin dosing induction algorithms are especially sensitive to this risk because their dose calculations are based on the most recent INR value.

www.Warfarindosing.org is a web application that uses algorithms based on clinical and pharmacogenetic information to dose warfarin therapy. It is used to initiate warfarin in approximately 100,000 patients worldwide each year, and is being evaluated in a multi-centered randomized controlled trial called Genetic Informatics Trial (GIFT).

The purpose of this study is to compare two methods of addressing an INR that is lower than anticipated: one that uses the current INR versus a signals and systems engineering approach (convolution method), which also accounts for dose estimates from the prior days of therapy.

Methods: We combined dosing information for days 5 through 11 of warfarin therapy from a cohort of 301 GIFT patients. We then plotted the therapeutic dose over the mean of the last two estimated doses as a function of the nth day's estimated dose over the mean of the last two estimated doses. Applying signals and systems engineering principles of data filtering, we created a convolution, or recalculation, of the estimated doses. This convolution was modeled after a spline function, and the optimal spline function was derived with three degrees of freedom using R programming software.

Results: The convolution method yielded a mean absolute error (MAE) reduction of 0.009 mg/day (p=0.032).

Conclusion: A data-driven convolution shows potential to improve the safety and efficacy of warfarindosing.org by correcting for post-analytical errors or spuriously low INR values. A pragmatic application of this research is that now a physician using warfarindosing.org will receive a pop-up alert if the new estimated dose is greater than what would be calculated by the convolution. Our approach highlights the theoretical importance of a dosing algorithm that is not independent of the prior dose estimates.
NEW YORK PODIUM PRESENTATION - RESEARCH Debapria Das

Development of Patient-Pathology Specific Aortic Root Model for Potential Risk Analysis of TAVR.

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Introduction: Paravalvular leakage after Transcatheter Aortic Valve Replacement (TAVR) is frequent and its severity has shown to be an important predictor of long-term mortality. Improper positioning of the replacement valve may provide the substrate for multiple complications including paravalvular leakage, valve embolism, and aortic dissection. A deeper understanding of the valve interactions with calcified tissue in the aortic root through patient-specific models may lead to better clinical practice by predicting both survival and quality of life post-TAVR. We hypothesize that such a model can be constructed and 3D printed with normal pre-procedural imaging.

Methods: CT datasets were used from a patient who experienced valve migration during a TAVR procedure at Stony Brook University Hospital. These DICOM images were used as input for the open-source software ITK-SNAP (www.itksnap.org), which implements a 3D active contour segmentation. A predefined range of intensity allows extraction of lumen boundaries and calcification regions. The vessel outer wall was obtained in a second phase by processing the lumen using an in-house code in MATLAB (MathWorks Inc., Natick, MA). In the final geometry of the aortic root, the main coronary branches were included to build a comprehensive vascular model for TAVR simulation. The model was imported in ANSYS Mechanical (ANSYS, Inc., Canonsburg, PA) in order to construct the mesh. The calcification regions were modeled as nearly rigid linear elastic whereas an anisotropic hyperelastic model was employed for soft tissue.

Results: The geometry of the aortic root was successfully meshed in ANSYS with a total of 4,719,327 elements and 6,865,219 nodes. The vessel wall thickness was set to 1.5mm. Our model features physiologically relevant variable thickness of the leaflets. Calcium deposits were embedded into soft tissue “pockets” within the vessel and valve wall and are not intersecting the surrounding tissue. The blood domain was extracted to fill the lumen and a portion of the left ventricle. The model is primed for dry and computational fluid dynamics analysis. A full-scale 3D model was printed for the surgeons for pre-operative clinical evaluation.

Conclusion: The model we have constructed includes patient-specific anatomy and is able to permit replication of pathological hemodynamic conditions using data from transesophageal echocardiogram. The use of pre-procedural imagining indicates that model construction and 3D printing can be successfully integrated with routine clinical workflow, thus suggesting better adoption if these models provide significant benefits to pre-operative evaluation and post-operative performance. Patient-specific models have many applications including risk analysis, procedure optimization, and personalized valve designs. The next step would be to construct an implicit scheme finite element model in ANSYS. Continuations of this model will lead to TAVR simulation and parametric studies to determine optimal valve placement.
OHIO PODIUM PRESENTATION - RESEARCH Kailin Yang, PhD

Radiosensitization of Glioblastoma Stem Cells by Targeting High-affinity Glucose Uptake

First Author: Kailin Yang, PhD, Co-Authors: William Flavahan, PhD, Samuel Chao, MD, Jeremy Rich, MD

BACKGROUND & PURPOSE: Glioblastoma (GBM) is a deadly form of brain tumor for which conventional treatments including radiation therapy are not curative. Increasing evidence suggests that GBMs contain cells similar to normal brain stem cells but form tumors. These cells – called glioblastoma stem cells (GSCs) – are usually a small fraction of the tumor but are important in tumor growth because of their ability to evade radiation and chemotherapy, promote new blood vessel growth to feed the tumor, and invade into normal brain. Recently, the role of metabolism in the growth of both stem cells and cancer cells supports a potential point of fragility that can be attacked to better treat these tumors. We showed that GSCs survive conditions with restricted nutrients by using a mechanism of high-affinity glucose uptake from normal nerve cells to outcompete for nutrients. In this study, we aim to understand how high-affinity glucose transporter (Glut3) promotes GBM radioresistance through maintaining tumorigenic hierarchical growth pattern, and to evaluate the therapeutic efficacy of inhibiting Glut3 to sensitize GSCs to radiation therapy.

Methods:

1. Examine the functional importance of Glut3 in tumorigenesis through xenograft mouse model. GSCs expressing Glut3 shRNA were implanted intracranially into immunocompromised mice. Tumor incidence, volume, and mice median survival were recorded.
2. Define the therapeutic benefits of down-regulating Glut3 on GSCs in conjunction with radiation. Glut3-targeting and control shRNAs were given to patient-derived GSCs in combination with radiation (3Gy). Cell survival assay was conducted 3 days after radiation to evaluate the effect of Glut3 knockdown.
3. Characterize the expression level of Glut3 in determining GBM patient survival. Based on TCGA (The Cancer Genome Atlas) database, the predictive value of Glut3 for GBM patient outcome was evaluated by examining the correlation between Glut3 expression level and overall survival.

RESULTS:

1. Glut3 is required for in vivo tumorigenesis of GSCs. In vivo tumor propagation assay with patient-derived GSCs demonstrated that targeting Glut3 using shRNA increased the survival of mice bearing human GBM xenografts relative to non-targeting shRNA (p<0.0004). This result demonstrated the essential role of Glut3 in maintaining GSC function in vivo.
2. Knocking down Glut3 sensitizes GSCs to radiation. Glut3 knockdown significantly decreased GSC survival after radiation compared to control (1.7 fold). This result revealed the function of Glut3 in promoting GSC survival after radiation therapy, consistent with its key role in GSC maintenance.
3. Glut3 expression level correlates with GBM patient survival. To evaluate the role of Glut3 in determining GBM patient survival, we generated Kaplan-Meier survival curves using TCGA dataset. Glut3 expression
informed poor prognosis, whereas other glucose transporters (Glut1/2/4) did not correlate with patient outcome.

**CONCLUSION & CLINICAL SIGNIFICANCE:**

Our results demonstrated that Glut3 plays a key role in enforcing GBM cellular hierarchy and promoting radiation resistance. This study provided scientific rationale to apply anti-glucose metabolism medication as potential adjuvant therapy to eradicate GBM and to develop imaging tools to detect GSCs in patients.
Contribution of demographics and psychological risk factors to the expression of acute stress reactivity following acute medical trauma

First Author: Edward W Ference III Contributing: Nate Harnett, James Bishop, Martin Setliff, Sherry Melton, David Knight, Amy Knight

Introduction: Currently, more than 7.7 million Americans, two thirds of them women, are being treated for Posttraumatic Stress Disorder (PTSD). This is prevalent, costly issue has been widely researched, yet the neural activity preceding the development of PTSD after acute trauma is largely unknown. This prospective study examined the relationship of the stress reaction to emotional, cognitive, and demographic variables following acute medical trauma. The goal of this research is to identify factors that mediate pathological and healthy emotion regulation, and translate this work into therapeutic strategies to provide targets for early intervention efforts. This goal will be accomplished by comparing self-reported trauma measures of affect, emotional reactivity, and attention between trauma-exposed individuals. The central hypothesis of this research is that trauma exposure will be associated with elevated self-reported psychological symptoms and decreased performance on attention, and will potentially be modulated by demographic factors.

Methods: 21 participants were recruited from the Acute Trauma Unit at UAB Hospital and completed a Posttraumatic Stress Diagnostic Scale (PDS), Psychosocial Risk Factor Survey (PRFS), and Connors' Continuous Performance Test II (CPT II). Correlation analysis was conducted on variables of interest, including demographic factors of gender, race, education, and estimated IQ.

Results: Endorsement of PTSD symptoms was correlated with depression, anxiety, and social isolation. African Americans had higher guardedness scores (an individual’s willingness to divulge personal information) than Caucasians (p=.044), suggesting potential bias in oral survey administration or an underlying cultural bias. Guardedness was not found to influence a willingness to disclose PTSD symptoms, while it lowered the severity of other mood symptoms endorsed. IQ scores correlated with social isolation (p=.020), which is consistent with prior research. Mood and PTSD scores were not consistently correlated with attention measures.

Conclusion: Results suggest that risk factors for emotional reactivity (depression, anxiety, social isolation) is related to the expression of acute stress (PDS) in the first 30 days following injury. Importantly, while we did find differences in ethnicity for emotional guardedness, this factor was not related to admission of an acute stress response. Contrary to our hypothesis, sustained attention was not reliably affected by the extent of symptoms reported.
ARIZONA POSTER FINALIST - RESEARCH Andrew Welch

The Novel Angiotensin (1-7) Cleavage Product Angiotensin (1-4) Increases Glucose-Stimulated Insulin Secretion and Cell Viability in Cultured Mouse Islets

Andrew Welch, Breanne Barrow, Sakeneh Zraika

Recent studies demonstrate a novel branch of the renin-angiotensin system present in pancreatic islets in which angiotensin converting enzyme 2 (ACE2) cleaves angiotensin I to generate the Mas receptor (MasR) agonist angiotensin (1-7) (Ang(1-7)). Upregulation of this ACE2/Ang(1-7)/MasR axis has multiple beneficial effects on islets including enhanced glucose-stimulated insulin secretion (GSIS) and increased islet cell viability, whereas down regulation of this axis produces islet secretory dysfunction and type 2 diabetes. While studies have focused on Ang(1-7) as the potential mediator of these beneficial effects, our lab has shown that peptidases present in the islet can further cleave Ang(1-7) to the tetrapeptide angiotensin(1-4) (Ang(1-4)).

It is unknown whether Ang(1-4) acts as an agonist or antagonist of the MasR. Therefore, the aim of our study was to determine whether Ang(1-4) functions as an agonist, increasing GSIS, insulin content, and islet cell viability. Islets were isolated from 10-week old C57BL/6J mice and cultured in the presence or absence of 1 nM Ang(1-4). After 48-hour culture, insulin secretion in response to 2.8 mM (basal) and 20 mM (GSIS) glucose, as well as islet insulin content were measured by ELISA (n=4). Islet cell viability was determined using an XTT assay which measures mitochondrial dehydrogenase activity in metabolically active cells (n=3).

These studies demonstrated that islets exposed to Ang(1-4) tended to secrete more insulin in response to 20 mM glucose compared to islets not exposed to the peptide [123.8±47.4 vs 81.7±25.3 pM/5 islets/h; p=0.16], while basal insulin secretion remained unchanged [26.1±3.5 vs 24.5±4.5 pM/5 islets/h; p=0.23]. This resulted in a 4.9±1.4 fold increase above the basal insulin response for Ang(1-4) exposed islets versus 3.0±0.7 fold with no peptide [p=0.09]. Further, insulin content did not differ between islets exposed to Ang(1-4) versus no peptide [62.9±7.0 vs 58.4±3.9 nM insulin/5 islets; p=0.66]. However, cell viability was significantly increased by 24±9% in islets exposed to Ang(1-4) [p=0.03]. These results show that Ang(1-4) increases GSIS and islet cell viability, suggesting it could be utilized as a novel therapeutic agent to treat β-cell dysfunction in type 2 diabetes.
AUSTRALIA - POSTER FINALIST - RESEARCH Vanessa W Wong

Quality of life and non-hospital management of elderly patients with type 2 diabetes mellitus

First Author: Vanessa W Wong Emily F Shen Ashley Bloom William L Browne

Introduction: Type 2 diabetes mellitus (T2DM) is a prevalent metabolic disease affecting multiple organ systems and impacting on patient quality of life (QOL). This impact on quality of life is especially significant in the elderly, in whom T2DM is more common and causes more complications. Poor quality of life can reduce the ability and motivation of patients to manage their condition, further increasing the burden of illness. However, the quality of life in this population is not well described. The adherence to medical and lifestyle guidelines in this population has not been previously reviewed. Therefore, in this study, our aims were to explore the quality of life of geriatric patients with T2DM and to see if these patients are managed according to the Diabetes Australia "General practice management of type 2 diabetes" guidelines.

Methods: We interviewed a cohort of free-living elderly patients with T2DM at Eastern Health hospitals, Victoria, Australia. We used the Problem Areas in Diabetes (PAID) questionnaire to assess QOL. Adherence to Diabetes Australia guidelines was determined by interview, examination, investigations and review of patient files. Results were analysed for statistical significance using the Mann-Whitney U test.

Results: We used measurement of HbA1c levels to estimate diabetic control and found that 38% of participants who had their HbA1c measured exceeded the recommendations for HbA1c. Two-thirds of patients (n=63) reported a minimal impact of diabetes on their QOL, while 7.4% reported a poor QOL due to their T2DM. The median PAID score (5) indicated a good quality of life for the average participant. Participants who reported a personal history of depression were more likely to report a poor quality of life. Concerns expressed by participants included burden of illness, satisfaction of treatment, impact of treatment and worries about the possibility of future complications. No patients fulfilled all management guidelines but 75% achieved at least half. Management guidelines that were most completely fulfilled were the recommendations that also applied to the non-diabetic population, including not smoking (99%), moderating alcohol intake (96%) and receiving vaccinations (83%). These were well known and understood by our participants. Guidelines that involved a time-consuming investigation, particularly urine collection for urine albumin creatinine ratio, were less completely achieved (13%).

Conclusion: Our study population of elderly patients with T2DM had a better QOL compared with studies of non-elderly patients with T2DM, consistent with our expectations. This was despite their incomplete adherence to guidelines for management of T2DM. Further studies using a larger population size are needed to confirm the observations.
CALIFORNIA POSTER FINALIST - RESEARCH Margaret Chi

Large Lipid-rich Plaques Detected by Intracoronary Near-infrared Spectroscopy are Associated with an Increased Risk of Future Acute Coronary Syndromes

Margaret Chi, Sarah Dionne, Drew Schmale, Andrew LaCombe, Andrew O’Brien, Ryan Farley, David Klungle, Stacie VanOosterhout, Samrath Singh, Mohsin Khan, Ryan Madder

**Background:** Intracoronary near-infrared spectroscopy (NIRS) is a catheter-based imaging technique developed and validated to detect lipid-rich plaques (LRP) in the coronary arteries at the time of coronary angiography. This study evaluates the association between large LRP detected by NIRS at non-stented sites and the occurrence of future acute coronary syndromes (ACS) requiring revascularization.

**Methods:** NIRS was performed in the target artery of 121 patients in single-center registry. Non-stented coronary segments were evaluated for large LRP, defined as a maximum lipid core burden index in 4-mm (maxLCBI4mm) = 500. Excluding events related to stented segments, multivariable Cox proportional regression analysis was performed to determine baseline characteristics associated with future ACS requiring revascularization.

**Results:** Among 121 patients (age 62.5 ± 11.2; 69% male) NIRS detected a large LRP in a non-stented coronary segment in 9.9% of patients. During 603 ± 145 days of follow-up, the cumulative rate of ACS requiring revascularization was 25.0% among those with a large LRP compared to 4.6% among patients without a large LRP (p<0.001). By multivariable Cox proportional regression analysis, the detection by NIRS of a large LRP at a non-stented segment at baseline was the only independent predictor of subsequent ACS (HR 8.5, 95% CI 2.0 – 35.8, p=0.004).

**Conclusions:** The present observations demonstrate that detection of large LRP by intracoronary NIRS imaging is associated with a greater risk of future ACS.
Utility of Routine 3-Minute Delayed Computed Tomography (CT) in the Trauma Setting

Neesha Mody, Jeanie Zhang, M.D., Mayil Krishnam, M.D.

Objective: To retrospectively evaluate the utility of 3-minute delayed computed tomography (CT) of the abdomen and pelvis in trauma patients, and to evaluate whether the routine trauma CT protocol can be improved to reduce radiation dose while maintaining diagnostic yield.

Materials and Methods: Institutional review board approval was obtained, and written informed consent was waived. A total of 665 adult patients (440 men, 225 women; mean age, 41 years; range, 18 - 99 years) were identified who were evaluated with CT abdomen and pelvis after sustaining trauma during a three months period in 2013. Routine trauma CT protocol at our institution includes an initial early portal venous phase scan (40 seconds) of the abdomen and pelvis, followed by a 3 minute delayed scan of the abdomen after intravenous contrast injection. The inclusion of the delayed scan is to produce a pyelographic phase for better detection of collecting system injuries. The radiologist’s report, including radiation dose reporting, and selected imaging findings were reviewed. Delayed scans were considered useful in diagnosing collecting system injuries when they either 1) identified a collecting system injury not seen on initial scan, 2) better characterized a collecting system injury, or 3) excluded a collecting system injury suspected on initial scan.

Results: Our data showed that 28.9 % (192 out of 665) trauma patients had positive traumatic findings on CT. Delayed scans were useful in excluding injury to the collecting system in 1.2 % (8 out of 665) patients. Most common traumatic findings were subcutaneous tissue injury (74), pelvic fractures (48), spine fractures (46), spleen injury (28), liver injury (24), and bowel injury (19). Only 0.45 % (3 out of 665) were found to have traumatic injuries to the collecting system, all diagnosed by initial scan. Initial portal venous scan carried a mean DLP of 16 mGy x cm and CTDIvol of 1153 mGy. Delayed scans carried a mean DLP of 12 mGy x cm and CTDIvol of 451 mGy, with effective radiation dose of 0.18 mSv.

Conclusion: Routine three minute delayed CT scans in trauma patients have low diagnostic yield, with about 1% of scans useful in excluding diagnosis of collecting system injuries. Delayed scans impose greater radiation exposure to the patient and delay patient care. The trauma CT protocol can be improved by performing selective rather than routine 3-minute delayed scans, thereby reducing radiation dose to the patient without compromising diagnostic yield.
Left Bundle Branch Block Heralds Increased Mortality Independent of Stress Test Results.

First Author: Tina Ramineni

Long-term outcomes due to left bundle branch block (LBBB) in patients referred for stress testing are not well investigated.

Methods: Records of 398 patients referred for stress echo at a single tertiary care center were reviewed. Demographic data and co-morbidities, including age, gender, cardiovascular disease (CAD), peripheral vascular disease (PVD), hypertension (HTN), and diabetes mellitus (DM) were collected. ANOVA, chi-square, and logistic regression analyses were performed. The mean follow-up length was 76+/-18 months.

Results: Left bundle branch block (LBBB) was observed in 11 patients (2.7%). LBBB was not associated with history of CAD and CAD risk factors: HTN, DM, PVD, or smoking. LBBB did not affect ability to reach target heart rate during stress test (9 vs. 12%, p=0.777). Patients with LBBB were more likely to have ischemic response to stress testing (6 vs. 2.2%, p=0.08) and experienced a 3-fold increase in long-term mortality (18.1 vs. 5.7%, chi-square p=0.086, Log-rank p=0.076) during the follow-up period. An association between LBBB and mortality was similar in magnitude to effects of ischemic response to the stress testing (10.6% mortality in ischemic patients vs. 5.2% in normal stress test, chi-square p=0.097, Log-rank p=0.095). The highest mortality was observed in patients with LBBB and no evidence of stress-induced ischemia (28.6%, p=0.021).

Discussion: Our observation suggests lack of association between LBBB and traditional coronary artery disease risk factors implying non-ischemic LBBB etiology in many patients. In patients referred for stress testing, LBBB confers increased risk of mortality regardless of stress test outcomes.
Impact of Inflammatory Biomarkers on Relation of High Density Lipoprotein-Cholesterol with Incident Coronary Heart Disease and Cardiovascular Disease

Tehrani DM, Gardin JM, Yanez D, Hirsch CH, Lloyd-Jones DM, Stein PK, Wong ND

**Background:** Inflammatory factors and low high density lipoprotein cholesterol (HDL-C) are associated with increased coronary heart disease (CHD) and cardiovascular disease (CVD) risk. Past studies have shown increased C-reactive protein are associated with an attenuation of the cross-sectional relation of HDL-C with prevalent CHD, but whether inflammation attenuates protection from CHD and CVD with high HDL-C is unknown.

**Objective:** Investigate the impact of inflammatory markers CRP, interleukin-6 (IL-6) and lipoprotein-associated phospholipase A2 (Lp-PLA2), individually and collectively, on the association of HDL-C with incident CHD and CVD.

**Methods:** We studied a longitudinal cohort of 3,888 older adults aged 65 to 98 without CVD from the Cardiovascular Health Study. HDL-C was categorized as >60, 40-60, and <40 mg/dL, CRP as <1, 1-3, and >3 mg/L, and IL-6 and Lp-PLA2 as gender specific tertiles. An additional inflammation index was created based on z-score sums of each individual's gender-specific CRP, IL-6, and Lp-PLA2 values. We calculated CHD and CVD incidence for each HDL/inflammation group and performed Cox regression, adjusted for standard CVD risk factors to examine the relationship of combined HDL-inflammation groups to incident CHD and CVD events occurring over a mean 11.1 and 10.3 year follow-up respectively.

Results: The unadjusted CHD and CVD incidence (per 1,000 person years) was higher for each tertile of the inflammation index and lower for each category of HDL-C. Similar trends were seen for unadjusted CHD and CVD incidence in relation to individual CRP and IL-6 inflammation tertiles. Compared to high-HDL/low-inflammation (referent), adjusted CHD Hazard Ratios (HR) were higher in those with mid-HDL/high-index (HR=1.41, p<0.01) and low-HDL/high-index (HR=1.46, p<0.01) groups. Increased CHD incidence was present in those with high-CRP (1.45-1.53, p<0.01) and high-IL-6 (1.36-1.61, p<0.05) irrelevant of HDL sub-grouping. Similarly, compared to high-HDL/low-inflammation (referent), adjusted CVD HRs were increased in those with high-CRP (1.30-1.47, p<0.01) and high-IL-6 (1.29-1.57, p<0.05) irrelevant of HDL sub-grouping. Similar associations were not seen with Lp-PLA2 for CHD and CVD events.

**Conclusion:** The cardioprotective relation of high HDL-C for incident CHD and CVD is attenuated by greater inflammation. Further study is needed to determine if inflammation’s relation to increasing risk at all levels of HDL-C is a direct one in both the coronary arteries and systemic vascular beds.
Quality Improvement for Advance Care Planning Completion Rates in a Community Clinic

Jules Vieaux, B.S., John MacMillan, M.D., Raminder Gill, M.D., and Benjamin Mansalis, M.D.

Introduction: There is substantial evidence that the medical treatment people would choose at the end of life is commonly different from the treatment they receive. Individuals’ preferences for where they wish to spend the end of their lives are also often not met. It is generally agreed that Advance Care Planning (ACP) and Advance Directives (AD) are useful tools to provide the mechanisms for ensuring individual autonomy at the end of life. In fact, the National Committee for Quality Assurance evaluates medical records for Patient-Centered Medical Homes to determine that patients either have an ACP offered or documented. Nevertheless, fewer than 1/3 of American adults have an AD. Many studies have elucidated factors associated with increased completion of ACP and barriers to completion, but few studies have examined how the healthcare system can increase completion rates.

The Lifelong Over Sixty Health Center (OSHC) is a Federally Qualified Health Center community clinic serving over 3000 geriatric patients from diverse socioeconomic backgrounds. Audits indicated the completion rate for ADs at OSHC was between 3-7%. A two-phase quality improvement pilot program was developed to determine the ideal workflow for increasing the rates ACP and ADs are offered to and completed by patients at OSHC.

Methods: During the first phase of the pilot program, we interviewed medical providers and staff to identify existing best practices and new strategies to improve the ACP process. The workflow was evaluated by scheduling and leading discussions with nine patients resulting in three completed ADs.

The second phase investigated quality improvement strategies to increase ACP completion rates. We evaluated multiple referral strategies while developing and refining a discussion script to introduce ADs to patients. We deployed provider and patient surveys to understand motivations and barriers to ACP. Finally, we developed an EMR documentation strategy to facilitate accurate tracking of results.

Results: Over nine weeks, 99 patients were introduced to ACP services and given a copy of an AD during a 3-5 minute discussion while in clinic for other appointments. Each patient was offered the option of a future follow-up discussion either in-person, over the phone, or in a group meeting. 32 patients requested additional information, with 20 completing in-person discussions reviewing an AD, 10 completing a discussion over the phone, and 7 completing ADs. EMR documentation noted a 1.8% increase in the offering of ACP services across the clinic.

Conclusion: Initial research findings informed recommendations for improved ACP services with validated discussion scripts, a refined clinic workflow and clinic staffing recommendations. Future plans include program expansion to additional clinic sites and regular performance tracking.
Predictive Variables of Optimal Performance and Approval of the Medical Residence Exam in Medical Students

Hector Lezcano

Introduction: Academic performance in students is typically expressed through qualifications and depends on multiple factors. Most universities rely on three aspects to predict academic performance: performance on tests of intellectual aptitudes, academic high school results and admission test scores to get into college. We aimed to determine the predictors of performance as a medical student and passing the residence entrance exam.

Methods: We performed a retrospective descriptive study, where the universe of study consisted of medical students of the University of Panama in a period that included the first half of 2000 through the second half of 2011 (N=1513). Using a 99% confidence level and 80% of power, we obtained a sample of 1110 graduates chosen through a stratified random sampling by year of graduation. We divided the variables into three categories: those related to the period prior to admission to the university (e.g. high school credits, being 5 an excellent note and 1 a poor note), during admission (e.g. admission test result as academic capacities test (ACT) and general knowledge test (GKT), both based on 100) and to egress (e.g. academic index, being 3 an excellent index and 1 a poor index). The statistical difference between notes by year of graduation were made using ANOVA and Welch test. We established two models to determine predictive variables through logistic and linear regression.

Results: Data for 1137 students was obtained. Generally, the average of high school credits was $M = 4.28$ ($SD = 0.34$), where no difference was found between years. Regarding ACT ($M = 66.5; SD = 12.4$) and GKT ($M = 69.0; SD = 10.8$), a significant difference was found in scores by groups ($p<0.01$). Moreover, a graduate takes 6.4 years ($SD = 0.23$) to complete the career. In residence exam the average was $74.54$ ($SD = 0.62$). Approximately 35% of applicants fail the residence exam.

Conclusion: According to our models regression, the best predictor of optimal performance as a medical student is the high school credits. The academic index is the main predictor to approve the residence test. A number of years to complete the career above of 6 is a negative predictor to obtain high notes in the residence exam.
COLORADO POSTER FINALIST - RESEARCH Jessica L Rice

Speckle Tracking Echocardiography to Screen for Pulmonary Hypertension in Chronic Obstructive Pulmonary Disease

First Author: Jessica L Rice BA, Amanda Stream MD, Mark Geraci MD, Brendan Clark MD, Jennifer Dorosz MD, R. William Vandivier MD, Todd M. Bull MD.

Introduction: Pulmonary hypertension (PH) is a common complication of chronic obstructive pulmonary disease (COPD) and is associated with increased morbidity and mortality. Echocardiographic measures as currently employed have poor predictive value for the diagnosis of PH in COPD. Lung hyperinflation makes it difficult to get adequate imaging windows for measurement of the tricuspid regurgitation gradient, which is highly dependent on proper image acquisition angle and is the primary means of estimating pulmonary artery pressure (PAP) by echocardiography. Right ventricular (RV) strain obtained by speckle tracking echocardiography (STE) is a measure of myocardial deformation which correlates with RV function, PAP, and survival in subjects with PAH. We hypothesized that RV strain estimates would be feasible and more readily obtained than estimated Right Ventricular Systolic Pressure (RVSP) by tricuspid regurgitation velocity in subjects with severe COPD, and that RV strain would correlate with invasive hemodynamic measurements.

Methods: Retrospective analysis of RV strain values using standard apical views from 54 subjects with severe COPD with echocardiogram performed within 48 hours of pulmonary artery catheterization were included in the analysis.

Results: Tricuspid Regurgitation was identified in 17 (31%), while RV strain was obtained for 44 (81%). Absolute values of RV strain correlated inversely with pulmonary vascular resistance (PVR) ($r^2=0.17$, p 0.02). Subjects with a PVR>3 Wood Units (WU) were compared to those with PVR = 3 WU. Median RV free wall strain for subjects with PVR = 3 WU was -23% (range -29 to -15) versus -20% for those with PVR >3 WU (range -23 to -12), p 0.05. A receiver operating characteristic curve demonstrated an RV free wall strain of -24% to be 92% sensitive and 42% specific for identifying PVR>3 WU (AUC 0.74).

Conclusion: Using STE, RV strain estimates are feasible in the majority of subjects with severe COPD. Absolute values of RV strain vary inversely with PVR and may improve screening for PH in subjects with COPD. Our results suggest that the limitations imposed upon routine echocardiographic screening techniques by severe COPD are significantly reduced or eliminated using STE without requiring additional studies or echocardiographic views.
FLORIDA POSTER FINALIST - RESEARCH Charles F Doerner

MOLECULAR STRUCTURE-FUNCTION RELATIONSHIPS FOR ENZYMATIC ACTIVITY OF BETA-CAROTENE 9',10'-OXYGENASE (CMO2)

First Author: Charles F Doerner Second Author: XIAOMING GONG Third Author: LEON HARDY Fourth Author: LEWIS RUBIN

Introduction: The three-dimensional structure of a protein has been shown to be determined by its sequence of amino acids. While the tertiary structure of a protein can be experimentally determined by X-ray crystallography, some proteins may not be entirely crystallized due to difficulties in the purification process. Computational methods, in these cases, must be employed in order to determine a proposed structure. Information derived from the primary structure may provide insight into a proteins form and function. Structure-activity relationships of the carotenoid cleavage enzyme CMO2 have not been elucidated. Consequently, we have performed molecular simulations to determine stable 3D structures of CMO2 and correlation with protein function.

Methods: Full-length CMO2 was mutated at predicted critical residues (H226, H286, H357, E465, H574) and the mutated proteins were expressed in vitro. Functional activity was measured by quantitative lycopene metabolism in E. coli and HEK293 cells. CMO2 and mutant structures were predicted using protein threading (RaptorX), resulting in 10 possible 3D structures. The highest and lowest ranked structures were chosen for further modeling and simulation with scalable molecular dynamics simulation (NAMD and VMD) programs. The first step is to find the local energy minimum by solvating the protein and running a minimization simulation. Next, the protein was heated to body temperature. Finally, the protein was equilibrated into its lowest energy state.

Results: The modeling and simulations of the best data set describes a structure containing four alpha-helices and several beta-sheets. The interior of CMO2 features an opening/cleft that conforms to substrate binding/cleavage site criteria. Mutations of the selected residues to alanine(s) decreased the root mean squares deviation (RMSD) function, indicating decreased CMO2 structure movement and stabilization. The bioinformatics results correspond with our finding that the expressed CMO2 mutants inhibit carotenoid metabolism in vitro.

Conclusion: In conclusion, these results localize the catalytic region of CMO2. Because CMO2 cannot be purified to sufficient concentration for x-ray crystallography, the exactly three-dimensional structure is unknown. However, through our statistical analysis, we have achieved a stable model with tertiary structure that conforms to protein folding shown to exist in other proteins of similar primary structure. This work should facilitate further investigations of metabolism of specific carotenoids in vitro and in vivo.
First Commercial Use of Drug Eluting Balloon in USA to Prevent Restenosis

First Author: Milan Patel, Mahir Elder

Peripheral vascular disease is a common condition with variable morbidity affecting mostly the elderly population. Based on incident rates, innovative endovascular procedures are needed in order to obtain revascularization of the obstructed vessels to prevent compromise of blood flow. The standard practice for a stenosed peripheral vessel is an atherectomy, angioplasty or stenting.

A standard angioplasty has a disadvantage of lower primary patency rates; and re-interventions are necessary due to restenosis. The stents are not a preferable intervention in femoral-popliteal arteries due to restenosis and limited flexibility. The Lutonix 360 drug coated balloon (DCB) Catheter represents the next advancement in angioplasty. The DCB delivers an optimal therapeutic dose of Paclitaxel to stenosed femoropopliteal vessels via a standard angioplasty balloon, after a minimum of 30-second inflation time. Paclitaxel is particularly well suited compared to other chemotherapeutic agents due to various physiologic reasons. It is highly hydrophobic and lipophilic. These physiologic properties allow paclitaxel to be readily absorbed into the arterial tissue where it binds to lipids and protein within cells and the interstitium.

It is an antimitotic agent that prevents microtubule deconstruction, and inhibits restenosis by preventing migration and proliferation of smooth muscle cells, inflammatory cells and fibroblasts. Paclitaxel blocks cells in the G2/M phase of the cell cycle; which reduces neointimal hyperplasia, prevents restenosis and improves patency of targeted region. A randomized trial was done to evaluate patency of a femoropopliteal vessel at 12 months in 476 patients. Lutonix DCB revealed 65.2% patency superior to control Percutaneous Angioplasty of 52.6%, indicating higher efficacy with DCBs [LEVANT 2 trial].

Paclitaxel has multiple hematologic, cardiovascular and respiratory side effects, which are not expected during local delivery with the Lutonix DCB.
FLORIDA POSTER FINALIST - RESEARCH Ashok Shiani

Degree of concordance between single balloon enteroscopy and capsule endoscopy for obscure gastrointestinal bleeding after an initial positive capsule

First Author: Ashok Shiani B.S. Javier Nieves M.D., Seth Lipka M.D., Ambuj Kumar M.D., MPH, Kerolos Fahmi M.D., Sahab Mustafa M.D., Patrick Brady M.D.

Introduction: In patients with obscure gastrointestinal bleeding (OGBIB) capsule endoscopy (CE) is the initial diagnostic procedure of choice. Often patients undergo single balloon enteroscopy (SBE) with both diagnostic and therapeutic intention after CE. Although SBE offers a therapeutic benefit, long procedure times, complexity, and invasiveness are drawbacks. We aimed to evaluate the diagnostic correlation between these two modalities after an initial positive CE finding.

Methods and Materials: We performed a retrospective review of 418 patients that underwent CE at our institution from 1/2010-5/2014. 95 patients were analyzed after selecting patients that underwent SBE originally after a positive CE result for the evaluation of OGBIB. Agreement beyond chance was evaluated using kappa coefficient. A p-value <5% was considered statistically significant.

Results: Mean age of our population was 65.8+-12.2 and was a female predominant group 57/95(60%). The most frequent positive findings were vascular lesions found on SBE in 31.6%, and on CE in 41.1%. There was a strong agreement when identifying active bleeding/clots kappa 0.97 (CI 0.92 – 1.03; p=<0.0001), and a moderate agreement when diagnosing vascular lesions kappa 0.41 (CI 0.21 – 0.61); p=<0.0001). There was fair agreement for ulcers 0.26 (CI 0.07 – 0.59; p=0.005). There was a low correlation between masses, polyps, and others. Most lesions were detected in the jejunum on CE (66.3%) and on SBE (37.9%).

Conclusion: CE and SBE have a strong agreement for active bleeding/clots, and a moderate agreement for vascular lesions. Since correlation between CE and SBE is not always optimal, patients without severe co-morbidities can be considered for balloon enteroscopy as the initial procedure. Further research should focus on methods to improve interpretation of CE and enhance the ability to evaluate the entire small bowel with SBE.
The Effect of Mindfulness Meditation on Brain Dynamics: A Pilot Study

First Author: Michelle Shnayder Advisors: Catherine Kerr, Ph.D., Monica Linden, Ph.D.

Mindfulness meditation has been reported to improve both physical and mental health. Understanding the cortical brain rhythms involved in meditation training could provide insight into how the brain processes information and techniques to improve focus and attention.

Somatosensory (SI) 7-14 Hz alpha rhythms are thought to function as a filter for the processing of irrelevant sensory inputs in primary sensory cortex. This filter creates an inverse relation between alpha rhythm and spatial attention, where alpha power is decreased in areas of SI that are attended to and increased in unattended locations. Meditation has been shown to enhance this top-down regulation of 7-14 Hz cortical oscillations, but only for brief periods of control. This study looked at the ability of three people in various degrees of meditation experience (a highly experienced meditator (+40 years), an intermediate meditator, and a non-meditaror) to maintain alpha rhythm modulation over 120 sec trials, as recorded by magnetoencephalography (MEG), while attending to their right or left hand. We suspected the most experienced meditator would be able to both raise his alpha power in SI and maintain this elevation more consistently than the other two participants.

While this subject demonstrated an increased ability to transiently raise his SI alpha power, he was no better at consistently maintaining that level than the other two subjects. These results suggest that alpha power alone and not temporal consistency is important in the attentional improvements arising from meditation training. This study is an important first step in understanding the neurologic implications of meditation.
GEORGIA POSTER FINALIST - RESEARCH Shabnam Gupta

Lumbar loading decreases the craniovertebral angle: a biomechanical model of pregnancy

First Author: Shabnam Gupta Second Author: Sean Bandzar Third Author: Essy Behravesh

Lower back pain (LBP) during pregnancy is ascribed to many biomechanical changes, most notably, an average increase in weight between 20 and 40 pounds. The shift in the body’s center of gravity anteriorly due to a growing fetus increases the moment arms of forces applied to the lumbar spine. LBP during pregnancy also has the potential to continue postpartum. The etiology of LBP is multifaceted, however, literature has established a link between LBP and poor head posture, specifically the craniovertebral angle (CVA). A smaller CVA indicates more forward head posture and decreased alignment of the entire spine. This study explores the effects of varying lumbar loads that mimic the pregnant state on an individual’s CVA.

Previous studies have measured a subject’s CVA using photographs. This study utilizes simple, affordable technology to measure the CVA. The CVAs of fifteen (n =15) students were examined under four loading conditions; no loading (control group), backpack weighing 10% of the individual’s body weight (BW), 15% BW, and 20% BW. The subjects were asked to wear the backpacks on their chest to mimic the lumbar loading seen during pregnancy. The resulting CVAs were recorded using a Nintendo Wii Remote and three infrared LEDs. One LED was placed in each of the following locations: on the subject’s tragus of the ear, on the C7 vertebrae, and at a position anterior to the C7 vertebrae. The LED coordinates were used to calculate the CVA. A one-way ANOVA test was conducted to assess if there were differences between the average CVAs of each test condition (p = 0.04). A post-hoc Tukey test was conducted to test for significance between each experimental condition and the control. The mean CVAs due to a backpack load of 15% and 20% BW were determined to be statistically different from the control (a=0.05).

The data suggests that lumbar loading during pregnancy can be inversely related to CVA. It also suggests that lumbar loading during pregnancy greater than 15% BW can have adverse effects on the spinal column as illustrated by the statistically significant decrease in CVA. This study is of particular interest because of its prognostic potential for attributing postpartum LBP to CVA. Future studies are warranted to determine baseline CVA in pregnant women and to investigate postpartum musculoskeletal complications associated with a decreased CVA during pregnancy.
GEORGIA POSTER FINALIST - RESEARCH Brendan P Lovasik

Geographic determinants of low pre-ESRD nephrology care in the United States

Brendan P. Lovasik, Hua Hao, Stephen O. Pastan, Howard Chang, Rachel E. Patzer

**Background:** Pre-ESRD nephrology care is crucial for optimizing clinical outcomes for patients with end stage renal disease (ESRD). Geographic variation of pre-ESRD nephrology care coverage has not been studied nationally.

**Methods:** A marginal mixed generalized estimating equation model was used to estimate the association of the proportion of patients within a facility who received pre-ESRD nephrology care coverage and facility-level neighborhood characteristics among 5,387 dialysis facilities across the US. SaTScan testing was utilized to detect geographic clusters of dialysis facilities with low pre-ESRD nephrology care coverage.

**Results:** Dialysis facilities in the lowest quintile of pre-ESRD nephrology care were geographically clustered in 5 distinct areas (P<0.05), including San Francisco, Los Angeles, Chicago, Miami, and Baltimore and along the corridors of Mississippi and Ohio River. (Figure 1) Facilities in the lowest quintile of pre-ESRD nephrology care were more likely to be located in inner cities compared to those in the highest quintile (45.8% vs 21.8%, OR=1.88, P=0.014). Lowest quintile facilities were significantly more likely to be in high-poverty neighborhoods (24.2% vs. 16.6%, OR=1.96, P=0.030). The proportion of racial minorities within a neighborhood was not associated with pre-ESRD nephrology care rates (P=0.929).

**Conclusions:** The proportion of patients receiving access to pre-ESRD nephrology care within a facility varies by geographic region. Policy makers and ESRD Networks should target these low-pre-ESRD facilities and regions to improve access to nephrologist care with interventions and specific pilot programs aimed at improving patient outcomes. Further examination of what factors make geographic regions better or worse at providing pre-ESRD nephrology care is warranted.
Phase I / II Trial of triplet regimen with Docetaxel,Oxaliplatin and Capecitabine in advanced gastric and gastroesophageal cancers

Kalaimani Elango, Prasad Eswaran, Kalaichelvi Kannan, Kavin Kaliappan, Mohammed Samiulla, Chidambaram Ramasamy, Balaji Nagarajan, Amit Dharmchand Jain, Amit Kumar Dey, Vignesh Gunasekaran, Mohankumar Doraiswamy, Ahmed Soukath, Koushik Shivakumar, Hariharan Sathishkumar

Background: Advanced and metastatic gastric cancers present at late stages and have very dismal prognosis. Many modifications have been tried for improving the prognosis. DCF/ECF are the regimen which has been established as standard in clinical trials, however they are limited by their toxicities.

Aim: We conducted a study to assess the maximal tolerated dose of docetaxel given at day 1 and 8 along with fixed doses of Oxaliplatin (day 1, 8) and Capecitabine (day 1 – 14), toxicity profile, response rate and efficacy of the triplet combination in advanced / metastatic gastric and GEJ malignancies.

Materials and Methods: Study was conducted in 2 phases. Phase I study assessed the MTD and Phase II assessed toxicity, response and efficacy of polychemotherapy. Escalating doses of docetaxel was tested in phase I design along with Oxaliplatin 50 mg/m2 (day 1, 8) and Capecitabine 625mg/m2 (day 1 – 14). MTD dose of Docetaxel was used in phase II along with the other two drugs for assessment of primary and secondary endpoints.

Results: Twenty four patients were evaluated in phase I design as per Modified Fibonacci series. The MTD achieved for Docetaxel was 40 mg/m2 given on day 1 and 8. On evaluation of twenty seven patients in phase II, hematological, neurological and biochemical toxicities were tolerable. Grade 3 diarrhoea and Hand Foot Syndrome were the most common toxicities. Overall response rates were 66.6%. Median progression free survival was 8.4 months.

Conclusion: The Maximal Tolerated Dose of Docetaxel was 40 mg/m2 (Day 1 and 8) administered along with Oxaliplatin 50 mg/m2 (Day 1 and 8) and Capecitabine 625 mg/m2 (Day 1 – 14). The regimen had proven to be efficacious with appreciable overall response rates, progression with tolerable and manageable toxicities.
Mycobacterium tuberculosis: Fluoroquinolones & Aminoglycosides- drugs in deception?

First Author: Swati Tyagi Second Author: Pratibha Sharma Last Author: Deepthi Nair

INTRODUCTION: To compound the problem of tuberculosis infection, there is increase in drug resistance due to indiscriminate use, leading to selection of mutations, viz. Multi-Drug Resistant (MDR-TB), Extremely Drug Resistant (XDR-TB) and Totally Drug Resistant TB (TDR-TB).

Widespread over-the-counter availability of fluoroquinolones (FQ) and aminoglycosides (AMG) owing to broad-spectrum of activity, oral efficacy and good tolerability. Blind therapy of infections leads to selection of resistant forms of tuberculosis strains, thus severely limiting treatment options. Additionally, their resistance is not routinely assessed and therapeutic failure is attributed to non-compliance to therapy. The present study was undertaken to evaluate of resistance pattern to FQ & AMG.

METHODS: Equal number of sensitive and multi-drug resistant archived isolates of Mycobacterium tuberculosis were tested to evaluate drug-susceptibility pattern, by Löwenstein–Jensen (L-J) and BacT/ALERT 3D proportion methods (bio MeCrieux, France); L-J method being taken ‘gold standard’. The 1st & 2nd line drugs tested: streptomycin, isoniazid, rifampicin, ethambutol; ciprofloxacin, ofloxacin, levofloxacin, amikacin and kanamycin.

RESULTS: Alarmingly, 10% resistance was observed towards 2nd line drugs: ciprofloxacin and ofloxacin in “sensitive” Mycobacterium isolates. No resistance observed towards rifampicin, levofloxacin, amikacin and kanamycin in sensitive isolates; 30% resistance observed towards ethambutol; 40% towards streptomycin and isoniazid.

Amongst MDR isolates 100% resistance was observed towards isoniazid and rifampicin; 77.8% to ethambutol; 55.6% to streptomycin and ciprofloxacin; 11.1% to ofloxacin and levofloxacin. No resistance observed towards aminoglycosides.

The BacT/ALERT 3D system correlated well with the L-J proportion (>90% correlation) for all drugs in sensitive MTB isolates and in 6 out of 9 drugs tested in MDR-TB isolates.

CONCLUSION: This preliminary study points at emerging FQ resistance towards FQs in ‘sensitive’ tuberculosis isolates. There is urgent need to address this issue among physicians to prevent indiscriminate use of antimicrobials against common ailments.
Nature's Double Edged Sword: The Ominous Response of Cancer Stem Cells to Chemo/Radiotherapy

First Author: Yiqing Xu, BS Second Author: Ling Li, MD, PhD Third Author: Xiaoqing Wu, PhD Fourth Author: Xinbao Hao, MD, PhD Fifth Author: Liang Xu, MD, PhD

Introduction: Relapse is a particularly feared outcome for cancer patients treated with chemo/radiotherapy. Emerging evidence suggests that cancer stem cells (CSCs), a small subpopulation of cells capable of self-renewal and differentiation, lie dormant during conventional chemo/radiotherapy and regrow after such therapy is discontinued. In our preliminary studies, we found that upon chemo/radiotherapy, bulk tumor cells were killed or inhibited, but the resistant CSCs increased in percentage.

We hypothesized that these quiescent CSCs serve as a reserve and are activated by a stress response mechanism to survive chemo/radiotherapy. Methods: CD44, CD133, and/or ALDH were used as markers to sort CSCs by flow cytometry from cell lines and primary tumors of human breast, pancreatic, and prostate cancer, before and after first-line chemo/radiotherapy. Changes in CSCs function and cell signalling were examined by real-time PCR, Western blot, reporter assays, clonogenic assay and tumorsphere assays in vitro. We studied the effects of CSC-specific therapy with anti-CD44 antibody in vivo with a human pancreatic cancer orthotopic model and a post-radiation tumor recurrence model in NOD/SCID mice.

Results: CSCs in human breast, prostate and pancreatic cancer were found to have high levels of Bcl-2 and CD44. Chemotherapy and X-ray radiation increased CSCs population (0.69% ± 0.06% to 4.09% ± 0.45% in pancreatic cancer cells post-radiation) and promoted CSC function even though the total tumor cells were reduced. Bcl-2 inhibitors chemo/radiosensitized cancer cells by inhibiting CSCs and inducing autophagic cells death by blocking Bcl-2-Beclin interaction, both in vitro and in vivo (p
Theranostic Treatment Option for Pancreatic Cancer

Purpose: Modern methods of pancreatic cancer diagnosis and treatment are severely lacking and have failed to provide effectual treatment options for patients inflicted with pancreatic cancer. The root cause of this inadequacy stems from the a-vascularized nature of pancreatic cancer, making traditional chemotherapeutics and cancer detecting contrast agents nearly obsolete. A potential solution to the targeting difficulties experienced when treating pancreatic cancer is through the implementation of nanotechnology, specifically ligand capped, theranostic nanoparticles. Nanoparticles have been a field of intense, growing research for decades and show great promise in the field of oncological research. We hypothesize that pH-responsive chitosan-capped mesoporous silica nanoparticles (MSNs) with the targeting ligand, urokinase plasminogen activator (UPA) will serve as theranostic agents for treatment and diagnosis of pancreatic cancer.

Methods: MSNs were synthesized by employing cetyl trimethylammonium bromide (CTAB), tetraethyl orthosilicate (TEOS) and chitosan through the sol-gel method. The synthesized MSNs were characterized by transmission electron microscopy (TEM) and zeta-potential measurements. Afterwards, Gemzar chemotherapeutic drug was encapsulated into these nanoparticles to observe the pH dependent release profiles in- vitro. Furthermore, MSNs were tagged with UPA to increase the binding efficiency of these nanoparticles towards the pancreatic tumor cells (S2CP9 and S2VP10). The binding efficiency of both tagged and non-tagged MSNs was observed at various pHs (7.4 to 6.5) by employing fluorescence microscopy, Odyssey infrared imaging and tissue phantoms. For that, various types of dyes were used, such as, rhodamine B and with indocyanine green (ICG). Finally, UPA-tagged MSNs with ICG were injected into mice infected with S2CP9 tumors cells to observe the distribution of these nanoparticles in-vivo by multispectral photoacoustic Tomography system (MSOT).

Results: TEM pictures showed that the synthesized MSN had a size around 120 nm. Zeta-potential measurements revealed that charge density of MSN dependent on pH. The release experiments showed that these nanoparticles were pH-sensitive because the release of Gemzar depended on the pH. Gemzar released ~2x the quantity from MSNs at pH 6.5 in comparison to pH 7.4. Fluorescence microscopy, Odyssey infrared imaging and tissue phantoms showed that uptake of MSNs by pancreatic tumor cells depended on the pH and tagging of UPA. Lowering a pH and tagging a ligand drastically increased the uptake of MSNs in pancreatic tumor cell in-vitro. Specifically in tissue phantoms, UPA-ICG loaded MSNs at pH 6.5 demonstrated 20X and 7X more cell signal than without ligand or at pH 7.4, respectively. Furthermore, UPA-ICG loaded MSNs were successfully detected in orthotopic pancreatic tumor of mice within 4 hours of imaging time by MSOT.

Conclusion: The results from this study illustrate a novel and efficient theranostic treatment option for pancreatic cancer involving the successful development of pH sensitive, UPA loaded, silica based nanoparticles (MSNs). MSNs were found to possess a heightened efficacy towards orthotopic cancer cells of multiple cell lines in both in-vitro and in-vivo study. The heightened efficacy of the MSNs was determined to be facilitated through the targeting methods of particle pH sensitivity and UPA ligand conjugation. With further analysis and implementation of this technology there is potential to revolutionize the treatment of pancreatic cancer and other metastatic disease.
Massachusetts Poster Finalist - Research Nathaniel Erskine

Multi-Decade Long Trends (1986-2009) in Duration of Pre-Hospital Delay in Patients Hospitalized with Acute Myocardial Infarction (The Worcester Heart Attack Study)

First Author: Nathaniel Erskine BA Co-Authors: Darleen Lessard MS Jorge Yarzebski MD, MPH Joel Gore MD Robert Goldberg PhD

Introduction: Prolonged delay between the onset of symptoms suggestive of acute myocardial infarction (AMI) and seeking treatment can reduce the likelihood of receiving early revascularization therapy. American hospitals have made substantial progress in shortening the length of time between the emergency room arrival of a patient with an AMI and receipt of reperfusion therapy; there is considerably less evidence, however, for a similar reduction in the time that it takes patients with an evolving AMI to present to the hospital. Using data from a population-based coronary disease surveillance study, we examined trends in, and characteristics associated with, extent of pre-hospital delay among patients hospitalized at all 11 medical centers in central MA with an AMI.

Methods: The study sample consisted of 6,750 residents of the Worcester, MA, metropolitan area hospitalized with AMI on a biennial basis between 1986 and 2009. We reviewed their medical records to collect information on demographic, medical history, and clinical characteristics.

Results: The mean age of this population was 67.3 years and 38% were women. Mean and median pre-hospital delays times, respectively, declined from 4.1 and 2.0 hours in 1986 to 3.4 and 1.9 hours in 2009. Linear regression analysis confirmed a statistically significant, but small, decrease in mean pre-hospital delay during this period. Between 1986 and 2009, the percentage of patients presenting to the hospital within 2 hours of the onset of their acute symptoms increased slightly from 46% to 51%. Women, patients who were older, did not complain of chest pain, and had a history of diabetes or angina were at greater risk for prolonged delay than their respective comparison groups (p < 0.005).

Conclusion: During the multi-decade long period under study, our results suggest a slight decline in the duration of pre-hospital delay in patients hospitalized with AMI in this large metropolitan area; however, the extent of delay in seeking timely medical care remains prolonged. Patients who are less likely to experience the classical symptoms of AMI, including women, older persons, and those with diabetes, experienced prolonged delay times. Our results highlight the need to promote greater awareness among the public about the symptoms of AMI and the importance of rapid care seeking behavior.
Multi-Decade Trends (1986-2009) in the Incidence and Hospital Case Fatality Rates Associated with Cardiogenic Shock in Patients Hospitalized With Acute Myocardial Infarction (The Worcester Heart Attack Study)

First Author: Nathaniel Erskine BA Co-Authors: Darleen Lessard MS Jorge Yarzebski MD, MPH Joel Gore MD Robert Goldberg PhD

Introduction: Cardiogenic shock is a leading cause of hospital mortality associated with acute myocardial infarction (AMI). Over the past several decades, the adoption of early revascularization and use of evidence-based guidelines has contributed to important improvements in the short-term survival of patients hospitalized with AMI. However, it is unclear whether these therapeutic advances have decreased the risk for developing cardiogenic shock, or improved short-term survival, in patients with AMI. We studied multi-decade long trends in the incidence and in-hospital case-fatality rates (CFRs) associated with cardiogenic shock (CS), and factors associated with the development of CS, in patients hospitalized with AMI in all 11 Central Massachusetts hospitals.

Methods: We examined the medical records of 12,015 residents of the Worcester (MA) metropolitan area hospitalized with a confirmed AMI on an approximate biennial basis between 1986 and 2009. Information on patient’s demographic, medical history, and clinical characteristics was abstracted.

Results: The mean age of the study sample was 69.6 years and 42.6% were women. Overall, 752 (6.3%) patients developed CS. The in-hospital CFR was 59.0% for patients with CS compared with 9.0% among those who did not develop CS. Between 1986 and 1997, the incidence rates of CS remained relatively stable (7.6% to 7.0%), with a marked decline in 2009 (3.7%). A linear regression analysis suggested a decreasing proportion of subjects who developed CS during the years under study (p = 0.04). Patients who developed CS were older, more likely to be female, and to have a medical history of heart failure and diabetes mellitus, compared with patients who did not develop CS (p < 0.05 for all comparisons). The in-hospital CFRs of patients who developed CS declined markedly over time, from 79.3% in 1986, to 58.1% in 1997, and to 31.0% in 2009.

Conclusion: The results of this community-based study suggest that the incidence of CS in patients hospitalized with AMI declined between 1986 and 2009, concomitant with a marked improvement in the hospital survival of these high-risk patients, during the years under study. While CS continues to be an important complication of AMI, our data suggests striking trends in both its incidence and short-term CFRs. This may be due to increased use of beneficial cardiac medications and revascularization procedures during the initial management of patients hospitalized with AMI.
MASSACHUSETTS POSTER FINALIST - RESEARCH Jonathan A Lim

EFFECT OF EARLY GOAL OF CARE MEETINGS IN THE MEDICAL INTENSIVE CARE UNIT ON READMISSIONS

Jonathan Lim, Student, Nicholas Bosch, MD, Sagar Patel, Renda S Wiener, MD, Michael Ieong, MD, Boston University School of Medicine, Boston, Massachusetts

Introduction: Identifying patients at risk for hospital readmission is an important goal to address preventable harm and cost in healthcare. Targeting select intensive care unit (ICU) patients may represent such an opportunity. The goal of this study was to evaluate the effect of early goals of care meetings (EGCM) on readmissions and was a part of a quality improvement (QI) project to improve EGCMs for ICU patients with anticipated poor prognosis.

Methods: Clinicians at Boston Medical Center implemented a QI project in 2012 for high risk ICU patients to receive EGCMs. Inclusion criteria for patients were any of the four following triggers present on ICU admission: 1.) cardiac arrest; 2.) stage III or IV cancer of any type; 3.) age greater than 80 with two or more organ system failures; or, 4.) anticipated ICU length of stay of greater than 5 days. EGCMs were defined as meetings occurring within 4 days of ICU admission, facilitated by an attending physician, and convened with the purpose of establishing goals of care with the patient or the patient’s healthcare proxy. As part of the QI intervention, critical care physicians received training on the patient triggers and the expected content of EGCMs, and were equipped with a new electronic medical record template for documentation. We performed a retrospective cohort study identifying pre-intervention (6 months pre-QI intervention) and post-intervention (6 months post-QI intervention) cohorts. Our primary outcome was hospital readmission within thirty days among those patients who were discharged alive from the index hospitalization. Secondary outcomes included use of palliative care consultations, decisions to withhold or withdraw care, and discharge to hospice during the index hospitalization.

Results: Among the 665 patients meeting one of the four triggers, after excluding 182 patients who did not survive to discharge, 255 remained in the Pre-Intervention cohort and 228 in the Post-Intervention cohort. EGCMs significantly increased following the QI intervention: 42/255 (16.9%) pre-intervention vs 65/228 (28.5%) post-intervention, chi-square P<0.05. Hospital readmission significantly decreased after the intervention (60/255, 23.5% Pre-Intervention versus 33/228, 14.5% post-intervention, P<0.05). Moreover, palliative care consults (9.8% vs 15.8%, p<0.05), decisions in the ICU to withhold or withdraw care (11.0% vs 17.5%, p<0.05), and discharges to hospice (5.5% vs 9.2%, p<0.05) all significantly increased after the intervention.

Conclusion: Hospital readmissions decreased after a QI intervention that successfully promoted earlier family meetings to promote goals of care discussions among ICU patients with a poor prognosis. We suggest that this is associated with discharges to hospice, palliative care consults, and decisions in the ICU to withhold or withdraw care resulting from these goals of care discussions. We plan subsequent cycles of the QI intervention to better understand how early goals of care meetings may contribute to decreasing readmissions.
Identification and Categorization of Medical Diagnosis Errors from a Hospital Risk Management Database

First Author: Leonard Rodman

BACKGROUND: Diagnosis errors represent the largest category of alleged malpractice cases in the published literature but remain largely unstudied because they are exceedingly difficult to detect and analyze. Although recent reviews of spontaneously reported cases and closed malpractice claims have improved our understanding of their causation, the prevalence and features of such errors in the larger pool of hospitals’ risk management databases has not been previously described.

METHODS: We retrospectively analyzed a large urban teaching hospital’s proprietary SQL-based risk management database to harvest cases of missed or delayed diagnoses. Cases were selected using the following search terms: “delay(ed)”,” “diagnosis”, “error”, “misread”, and “miss(ed)”. Cases were then screened by a student and in a second pass by two or more experienced internists. Confirmed cases of diagnosis error were classified using the DEER (Diagnosis Error Evaluation and Research) taxonomy tool.

RESULTS: Out of 1,594 new cases reported to risk management over a 20 month interval, 420 were selected by text query. Manual review by a student removed 270 cases as appropriate per training, and detailed physician review of the remaining 249 cases identified 75 definitive missed or delayed diagnoses. Among these 75 cases, cancer was the most common final diagnosis (32%), followed by fracture (9%). The majority of errors were related to laboratory/radiology testing (54%), followed by physician assessment (28%).

CONCLUSION: Systematic analysis identified numerous cases of diagnosis error, yielded useful insights into their causation, and led to modification of the case reporting and tracking system. It is our belief that this methodology is more efficient than random case finding, and has potential use both clinically and in future research to improve detection, understanding, and prevention of future diagnosis errors.

Previous Presentation: Identification of Diagnosis Errors from a Hospital Risk Management Database. Society of General Internal Medicine Annual Meeting. Data updated since presentation.
The Effect of BMI in Time to Target Temperature in Post-Cardiac Arrest Therapeutic Hypothermia

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Introduction: Controversy surrounds the optimal time to target temperature (T2T) for induction of post-arrest therapeutic hypothermia (TH). While most protocols strive for ‘as quickly as possible’, little is known how baseline patient factors affect T2T. We investigated the relationship between body mass index (BMI) and T2T.

Methods: This was a retrospective chart review of adult patients who suffered non-traumatic cardiac arrest and were treated with TH at a large, community hospital between January 2009 and June 2013. The TH protocol was consistent among all patients, initiated as soon as possible after arrest, and target temperature (33.5°C) was achieved as quickly as possible. Demographics and variables were collected as part of a quality improvement database. Good neurologic outcome was defined as cerebral performance category (CPC) score of 1 or 2.

Results: During the study period 171 patients were included and 54 (31.6%) survived to discharge. The mean age was 62.5 (SD 15.8) and 109 (63.7%) were male. BMI was normally distributed with a mean of 30.6 (SD 8.8). The overall mean T2T was normally distributed with a mean of 344 minutes (SD 191 minutes). Linear regression indicated that increasing BMI was associated with an increased T2T (F=12.56, p-value <0.001).

Conclusions: A patient with a higher BMI took a longer time to attain target temperature in our cohort. Current recommendations for post-arrest care include reaching target temperature as quickly as possible. With this in mind, adjunctive elements may need to be added to the TH protocol for patients with a higher BMI.
Bilateral Breast Reduction: An Investigation Into The Complication Rate in Obese Women

Anna Pavlov, M.S. Erin Smith, M.S. Erica Hutcheson, M.D. Peter Arnold, M.D., PhD

Introduction: Bilateral Breast Reduction (BBR) surgery improves the quality of life in women with macromastia. There is discrepancy in the literature on the maximum BMI that is safe for operating, with many physicians avoiding surgical candidates with a BMI greater than 30. We hypothesize that it is safe to operate on obese women with a BMI up to 40.

Methods: In this retrospective cohort study, we examined the major and minor surgical complication rate in 60 women who underwent BBR by a single surgeon using an inferior pedicle/Wise pattern technique over a two-year period. The sample consisted of 13 women with a BMI less than 30, 34 women with a BMI between 30 and 40, and 13 women with a BMI greater than 40.

Results: The minor complication rate was 31% for BMI <30, 32% for BMI 30-40, and 54% for BMI >40. Though there was a 22% difference in the minor complication rate between obese women with BMI 30-40 and BMI >40, Fisher’s exact test revealed no significant difference (p=0.1968). The major complication rate was essentially the same for all groups, being 8% for BMI <30, 6% for BMI 30-40, and 8% for BMI >40 (p=0.9999).

Conclusion: In this study, we show that obese women with a BMI <40 have similar surgical complication rates as non-obese women, but the complication rate increases in women with BMI >40. The low rate of major complications in all patients likely represents reducing operative variables in both surgical planning and in the procedure itself rather than a relationship to body weight. Though the results were not statistically significant, increasing the sample size will increase study power and likely reveal a difference. Despite the lack of statistical significance, these findings prove clinically relevant for risk stratification when evaluating a patient for referral to a plastic surgeon for breast reduction surgery.
Plasma Metabolomic Markers Associated with Cognitive Performance During Aging: the Baltimore Longitudinal Study of Aging

First Author: Brittany Simpson BA Kim Min MSci, B Gwen Windham MD MHS, Luigi Ferrucci, MD PhD, Michael E Griswold PhD, Christina Legido-Quigley PhD, Madhav Thambisetty, MD PhD

**Purpose:** Identification of blood biomarkers predictive of early changes in cognitive performance in older individuals may accelerate the development of novel disease-modifying treatments by targeting those at greatest risk for Alzheimer disease (AD). Using a multi-platform metabolomics approach (liquid chromatography-mass spectrometry and nuclear magnetic resonance), we recently reported that plasma from AD patients showed lower concentrations of three phosphatidylcholine (PC) molecules relative to healthy controls. In this study, we extend these findings by investigating associations of plasma concentrations of PCs [PC16:0/20:5; PC16:0/22:6; PC18:0/22:6] with cognitive performance in non-demented older individuals in the Baltimore Longitudinal Study of Aging neuroimaging substudy (BLSA-NI).

**Methods:** Plasma PC concentrations [PC16:0/20:5 (PC1620); PC16:0/22:6 (PC1622); PC18:0/22:6 (PC1822)] and cognitive performance [California Verbal Learning Test (CVLT), Trails A&B, and the Mini-Mental State Exam (MMSE)] were measured in BLSA-NI participants who were non-demented at baseline (n=108, age 49-89 yrs, follow-up over 7.7 years). Associations of PCs with cognitive decline were examined using mixed-effects linear regression. PC associations with progression to AD/mild cognitive impairment (n=22) were examined using logistic regression. Models were adjusted for baseline age, sex, education, and APOE genotype.

**Results:** Lower baseline PC concentrations were associated with worse baseline memory (b with 95% confidence interval subscripts: CVLT long delay recall: PC1622: -1.38 -0.78 -0.18 p=0.010 and PC1822: -1.33 -0.74 -0.15 p=0.014; CVLT short delay recall: PC1620: -2.01 -1.15 -0.30 p=0.008, PC1622: -1.49 -0.85 -0.20 p=0.010, and PC1822: -1.48 -0.84 -0.21 p=0.010; CVLT total recall: PC1620: -7.40 -4.39 -1.38 p=0.004, PC1622: -5.54 -3.28 -1.01 p=0.005, and PC1822: -3.31 -2.07 -0.82 p=0.007). However, decreasing baseline levels of all markers were associated with a trend for better cognitive performance over time. No associations were observed with Trails A&B or MMSE. There were no significant associations between PC concentrations and subsequent conversion to AD/MCI.

**Implications:** Lower plasma concentrations of the candidate AD biomarkers, PC1620, PC1622 and PC1822 are associated with poorer memory performance in non-demented older individuals. However, lower plasma concentrations may be associated with improved verbal memory over time suggesting a differential association of our PC markers and cognition. Altered levels of these metabolites may be an early feature of dysregulated PC metabolism and brain functioning occurring in cognitive aging.
MISSISSIPPI POSTER FINALIST - RESEARCH Steven Wilkening

MRI predictors of cognitive decline over 20 years

First Author: Steven R. Wilkening B. Gwen Windham, Samantha Seals, Laura Coker, David Knopman, Rebecca F. Gottesman, Mike Griswold, Tom Mosley

Background: Subclinical cerebrovascular and neurodegenerative features on brain MRI are associated with cognitive status and dementia risk. We examined the effects of subclinical MRI features on decline in cognitive functioning in a population-based sample of predominantly middle-aged adults followed over 20 years, longer than any similar study.

Methods: A subset of 1835 participants of the Atherosclerosis Risk in Communities (ARIC) study (aged 50-73 yrs, mean=63; 40% men; 50% black) underwent brain MRI in 1993-95. MRI features were defined as high-grade white matter hyperintensities (hgWMH ≥3 on 0-9 scale), ventricular size (hgVS, ≥4), and sulcal size (hgSS, ≥3) and any infarct ≥3mm. Cognitive function was measured over 20 years across five visits by the Delayed Word Recall Test (memory), Digit Symbol Substitution (DSS; processing speed), and Word Fluency (WF; language). These scores were also used to create a global composite score. Linear mixed effects models with random intercepts were used to assess associations between MRI features and decline in standardized cognition scores over 0-10, 10-20 and 0-20 years adjusting for age, race, sex and education. Those with intervening clinical stroke were excluded.

Results: Cognition declined over 20 years in all groups. The 0-20 year decline in global cognition was faster in those with hgWMH (-1.31 sd/20yrs) vs without (-1.05 sd/20yrs), difference=-0.26 (95%CI: -0.50,-0.01), as well as the 0-20 year decline in WF for those with infarcts ≥3mm vs without (-0.48 vs -0.30), diff=-0.18 (-0.34,- 0.01). From 0-10 years, faster declines in DSS were observed for those with hgVS vs without (-0.36 vs -0.23 sd/decade), diff=-0.13 (-0.23,-0.03). However, from 10-20 years, those with hgVS showed slower declines than those without (-0.48 vs -0.68 sd/dec), diff=0.19 (0.02,0.36). No other relationships were statistically significant.

Conclusion: Cerebrovascular features (WMH and infarcts ≥3mm) were related to steeper declines in cognitive functioning over 20 years. Relationships for markers of atrophy (VS & SS) were mixed, potentially due to floor effects or differential attrition.
Targeted Delivery of Phosphodiesterase Inhibitors to Erythrocytes: Implications for the Treatment of Vascular Disease in Type 2 Diabetes

Weston R. Gordon, Elizabeth Bowles, Randy S. Sprague, MD

In skeletal muscle, when Erythrocytes (RBCs) are exposed to low O₂, they release both O₂ and the potent vasodilator, ATP, permitting these cells to alter distribution of perfusion to meet tissue O₂ need. However, in humans with Type 2 Diabetes (DM2), ATP release from RBCs in response to low O₂ is lost. This defect could contribute to the associated peripheral vascular disease (PVD).

A signaling pathway for low O₂-induced ATP release from RBCs that requires increases in cAMP that are regulated by Phosphodiesterase 3 (PDE3) has been defined. Although the use of the PDE3 inhibitor cilostizol (CILO) in DM2 is attractive, side effects limit its use. PDE3 can also be inhibited by cGMP, a cyclic nucleotide that is regulated by PDE5. The aims of this study were to 1) construct liposomes containing the PDE3 inhibitor, CILO, and determine if the directed delivery to DM2 RBCs restores low O₂-induced ATP release and 2) determine if a PDE5 inhibitor, zaprinast (ZAP), also rescues low O₂-induced ATP release from DM2 RBCs.

Blood was obtained from healthy humans (n=7) and humans with DM2 (n=10, hemoglobin A1c=8±1). RBCs were isolated by centrifugation, washed, diluted to a 20% hematocrit and equilibrated with 15% O₂, 6% CO₂ (pO₂=107±5 mmHg; normoxia) in the presence of either empty liposomes or liposomes containing CILO (n=6), or ZAP (10µM,) or its vehicle dimethylformamide (DMF) (n=4). The gas was then changed to 0% O₂, 6% CO₂, (pO₂=10±1 mmHg; low O₂). Liposomes were made of dimyristoylphosphatidylcholine. ATP was measured by the luciferin-luciferase technique.

In healthy human RBCs ATP release increased from 13.9±2.3 to 25.2±4.6 nmoles/4x10⁸ RBCs with exposure to low O₂ (empty liposomes, n=7, P<0.01). In contrast, when RBCs of humans with DM2 were incubated with empty liposomes ATP levels did not increase (15.4±1.4 vs 14.7 ± 1.1 nmoles/4x10⁸ RBCs (n=6). The defect in ATP release was rescued in DM2 RBCs by incubation with CILO-loaded liposomes with ATP increasing from 15.6±1.5 to 26.6±1.4 nmoles/4x10⁸ RBCs (n=4, P<0.05). Similarly, following incubation of DM2 RBCs with ZAP, low O₂-induced ATP release increased from 9.3±2.5 to 20.7±3.6 nmoles/4x10⁸ RBCs (P<0.01).

In summary, both directed delivery of a PDE3 inhibitor to RBCs by liposomes and administration of a PDE5 inhibitor rescue low O₂-induced ATP release from DM2 RBCs. Restoration of this function permits DM2 RBCs to participate in the regulation of perfusion to meet tissue O₂ need and suggests new approaches to the treatment and/or preventing of the peripheral vascular disease of DM2.
NEPAL - POSTER FINALIST - RESEARCH Prajwal Dhakal

Eculizumab in Transplant-Associated Thrombotic Microangiopathy (TA-TMA)

First Author: Prajwal Dhakal Second Author: Smith Giri Third Author: Ranjan Pathak Last Author: Vijaya Raj Bhatt

Introduction: TA-TMA is a rare entity with no standard of care and high mortality despite the use of plasma exchange. We analyzed the efficacy of eculizumab in this setting.

Methods: Inclusion criteria included TA-TMA occurring after solid-organ or stem cell transplant (SCT) and use of eculizumab. Patients with a confirmed diagnosis of atypical hemolytic uremic syndrome and paroxysmal nocturnal hemoglobinuria were excluded. Using search terms, all such cases indexed in Pubmed (English language only) by November 2014 were reviewed. The bibliography of each relevant article was searched for additional reports.

Results: A total of 26 cases met the criteria. The median age was 33 years (range 2-61); 53% were male. TA-TMA occurred after SCT (35%), predominantly allogeneic SCT (n=7); or solid-organ transplant (65%), predominantly renal transplant (n=7). Donor status included matched (47%) or unmatched donor (53%). Cyclosporine or tacrolimus was used as prophylaxis in 96% of cases. Nonetheless, graft versus host disease occurred in 83% of allogeneic SCT, and graft dysfunction or rejection occurred in 29% of solid organ transplants. ADAMTS 13 levels were normal or only mildly decreased (>10%) in all cases. The median interval between transplant and TA-TMA diagnosis was 41 days (range 3–390). After TA-TMA diagnosis, following drug adjustments were made: discontinuation of cyclosporine or tacrolimus in 45% (with initiation of sirolimus in 2 patients), dose reduction in another 27%, continuation of the drugs in 23% and switch from cyclosporine to tacrolimus in remaining 5% of cases. Additionally, plasma exchange was performed in 42%, dialysis in 7% and both plasma exchange and dialysis in 1% of cases. The median interval between transplant and initiation of eculizumab was 63 days (range 11–512). A median of 5.5 doses (range 2–21) of eculizumab was utilized with response occurring after a median of 2 doses (range 1-18). Ninety-two percent of the patients recovered with the use of eculizumab but the rest died. At a median follow-up of 52 weeks (range 3-113), the survivors were doing well.

Conclusions: The majority of the patients in our study developed TA-TMA in the setting of calcineurin inhibitors and absence of severe deficiency of ADAMTS-13. Patients were initially treated with discontinuation or dose reduction of calcineurin inhibitor with or without plasma exchange. Eculizumab was often utilized after the failure of the initial therapy. This approach improved the condition in 92% of patients who were alive at 1-year follow-up. These results are promising compared to high mortality traditionally observed in TA-TMA. Within the limits of this retrospective analysis, our study demonstrates that eculizumab may be effective in the management of TA-TMA and may improve survival.
NEVADA POSTER FINALIST - RESEARCH Bonnie Lo

Antimicrobial Properties of Lichen Parmelia Vagans

B.L. Lo and V.A. Bondarenko

Introduction: Approximately one quarter of all prescription drugs contain active ingredients of plant origins. Studies have shown that the secondary metabolites of lichen are unique and can exhibit antimicrobial activity. The purpose of this project is to analyze antimicrobial properties of the secondary metabolites of lichen *Parmelia vagans* collected from the semi-deserts of Russia.

Methods: Various extracts of the lichen *Parmelia Vagans* were prepared using optimal combinations of hydrophobic and hydrophilic solvents. We assessed their antimicrobial activity against both gram positive and gram negative bacteria – *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*. Acetone has been chosen for preparative extraction because it yielded the highest antimicrobial activity. The extract was dried and the dry pellet was dissolved in DMSO. We utilized colorimetric cell survival assays to determine the minimum inhibitory concentrations of the extract against the four strains of bacteria listed. Solid medium assays were conducted using disc diffusion tests. Thin layer chromatography was used for preliminary isolation of secondary metabolites.

Results: We found that under our experimental conditions, all bacteria strains were susceptible to the broad spectrum antibiotic streptomycin, except for *E. faecalis*. Our acetone extract of *Parmelia vagans* successfully inhibited the growth of *E. faecalis* and *S. aureus* but had little to no effect on *E. coli* and *P. aeruginosa*, contrary to previous publications using extracts obtained from other *Parmelia* species. This finding indicates that our lichen species likely contains different antimicrobial secondary metabolites.

Conclusion: Future experiments will be conducted to provide further detailed analysis of *Parmelia vagans* extract in order to characterize the active antimicrobial metabolites responsible for the inhibition of bacterial growth. Novel antibiotics derived from lichen may hold vast medicinal potential and a viable means of alleviating the growing problem of drug resistant bacteria.
NEW JERSEY POSTER FINALIST - RESEARCH Elizabeth S John

Colorectal Cancer Screening Health Education Materials – How Effective are Online Education Sources?

First Author: Elizabeth S. John Second Author: Ann M. John Third Author: David R. Hansberry, M.D., Ph.D. Fourth Author: Prashant Jacob Thomas, M.D. Fifth Author: Christopher Deitch

Introduction: Colon cancer is the third most common cause of cancer death in the United States, with approximately 136,830 new cases being diagnosed annually. Various diagnostic tests, such as colonoscopies, flexible sigmoidoscopies, fecal occult blood tests (FOBT), CT colonoscopies, and virtual colonography, are utilized to screen for and diagnose colon cancer. The Internet has become a prominent tool patients utilize for online health information to garner a more comprehensive understanding of their conditions. This study investigates the readability of online patient education articles about five common colon cancer screening tools – colonoscopy, flexible sigmoidoscopy, FOBT, CT colonoscopy, and virtual colonography – to determine if they are written at a grade level that will facilitate patient understanding.

Methods: The five tests were searched online, and the readability levels of the top twenty results for each test were analyzed. One article was eliminated from analysis because the text was too short. Scientific literature and articles on patient blogs or forums were excluded as well. Ten validated readability scales were used to measure the grade levels of each of the articles. One-way ANOVA and Tukey Honestly Statistically Different (HSD) post hoc analyses were performed on all the results to determine if there were any statistically significant differences among the readability of the literature on the five diagnostic tests.

Results: The 99 articles were collectively written at an 11.9 grade level, with none of the articles written below a 7th grade level. There were significant differences among the five categories of articles F(4,77) = 4.33, p = 0.0032 with CT colonoscopy and virtual colonoscopy written at a more difficult level compared to FOBT.

Conclusions and Relevance: As approximately 84 million American adults use the Internet to search for health and medical information, with over 70% of patients reporting that the information they garner from the Internet influences their treatment decisions, it is imperative to investigate the readability of online health information (2). The online articles in this study were all written at much higher grade levels than the NIH’s and AMA’s recommended 3rd to 7th grade levels (3-4). Because online health information is becoming a more prevalent aspect of patient care and compliance, patients could significantly benefit from this modality of information if it were written at a level that would facilitate understanding.

References:

NEW MEXICO POSTER FINALIST - RESEARCH Jessica Zimmerberg-Helms

EFFECTIVENESS OF THROMBOPHILIA TESTING: TESTING TO A FAULT?

Jessica Zimmerberg-Helms MS II, Taylor Goot, M.D., Allison Burnett, Pharm D., and Patrick Rendon, M.D.

Introduction: Thrombophilias can occur from a variety of inherited and acquired abnormalities. Although patients with these abnormalities of the coagulation pathway often have a higher propensity to develop venous thromboemboli (VTE), the risk for developing a VTE is not fully dependent on the existence of an acquired or genetic abnormality. The question then remains, in the event of a VTE, when is testing indicated for a potential thrombophilic pre-disposition? The standard reasons to consider testing are to: a) Look for an underlying cause of an unprovoked VTE; b) Assess the probability of a repeat event thereby guiding duration of anticoagulation therapy; and c) Identify asymptomatic family members with an underlying predisposition to thrombophilia who might benefit from thromboprophylaxis or genetic counseling. In an effort to improve testing efficiency, the hypercoagulable panel order set (HCPAN), a set of 8 tests indicated for inherited thrombophilia, was instituted at the University of New Mexico at the outset of induction of the electronic medical record. However, we hypothesize that the HCPAN is being utilized outside of guideline-directed diagnostic utility.

Methods: A list of 600 HCPAN tests from October 2012 to November 2013 was generated from the TriCore laboratory historical database. This included all adult inpatient and outpatient instances. We conducted a manual chart review of each patient, evaluating risk factors for VTE, the rationale for ordering the HCPAN, and the level and service of the ordering provider. The protocol was approved by the Institutional Review Board for the UNM School of Medicine.

Results: Preliminary data indicate minimal correlation with ordering the panel and the status of the thrombophilic event. Out of the 50 patients analyzed, 42% of the charts surveyed ordered the HCPAN for a VTE that was clearly provoked. 71% of the panels were drawn while on one or more anticoagulants were present. Furthermore, 62% of HCPAN tests were ordered in the presence of an active thrombus.

Conclusion: The data indicates that the majority of HCPAN tests are being ordered outside of recommended guidelines, either because they are being ordered for a provoked clot, in the presence of anticoagulant, or in the presence of an active clot. Furthermore, our preliminary results also indicate that the HCPAN at UNM Hospital encompasses a variety of tests which appear to have been ordered in their entirety when only a small number of tests were indicated, and that the reason for this testing was often not documented in the chart. This, along with the evidence that the majority of testing is not in accordance with current guidelines, establishes that hypercoagulability testing is an area which may benefit from a quality improvement intervention.
Categorizing Neonatal Deaths: A Cost-efficiency Analysis of Resource Expenditure in U.S. and Filipino Neonatal Intensive Care Units (NICUs)

Maria Battaglia, Dr. Ceres Baldevia, Dr. Marilyn Fisher

The Neonatal Intensive Care Unit is an environment where some of the most extreme measures are taken to treat sick newborns. While this often results in newborns getting the expensive life-saving treatments that allow them to survive, it is also a place where countless resources may be spent with ultimate patient death. Previous studies have looked at resource expenditures based on cause of death in individual hospitals, but this study compared these data from two culturally disparate NICUs. This project examined the cost efficiencies of two NICUs in Albany Medical Center (AMC, Albany, United States) and Corazon Locsin Montelibano Memorial Regional Hospital (CLMMRH, Bacolod, Philippines), comparing the patterns of resource expenditure. This was a cross-cultural comparative study using retrospective chart review over a two-year period, examining medical records from 2011 and 2012 deaths. Deaths were categorized by cause and mode of death, using cost of medical care and length of stay as primary outcome measures. There were 92 deaths at AMC and 727 deaths at CLMMRH. Eight of the 727 NICU deaths at CLMMRH were excluded from the study because of incomplete records. The NICU mortality rates were 6% at AMC compared to 35% at CLMMRH in 2011 and 2012. Modes of death for neonates at AMC included treatment was either never initiated (43%) or treatment was withdrawn (41%). This is compared to CLMMRH, where treatment was withheld (67%) or neonates received unsuccessful cardiopulmonary resuscitation (33%). At AMC, previability accounted for 39% of neonatal deaths, followed by genetic syndromes (12%) and sepsis (8%). At CLMMRH, sepsis accounted for 37% of neonatal deaths, followed by respiratory distress syndrome (24%) and previability (10%). Infants with sepsis as the cause of death had the highest median hospital costs in both NICUs. The mean length of stay for NICU deaths was 13 days at AMC versus 3 days at CLMMRH. We found that causes of death vary considerably between the NICUs at AMC and CLMMRH. Resources were observed to play a direct role in the ability of the NICUs to spend both money and time treating these neonates. AMC’s vast resource availability may have driven an increased use of resources to treat neonates with futile situations. The outcomes of these neonates may have been similar to that which would have occurred had resource usage been more tightly monitored. At CLMMRH, resources appeared to be the limiting factor for treating neonates. If certain specific resources such as ventilators had become available, and there were earlier recognition of sepsis with prompt antibiotic administration, then there may have been a marked improvement in mortality rates. This study used both cost of treatment and length of stay as resource measures to gain a better understanding of the differences between two different communities and their approaches to interventions.
Pilot Medical Education Course Teaches Students About Health Justice Advocacy: An Educational Intervention Study.

*Tehreem Rehman, *Robert Rock, Kali Cyrus, MD, Roberto E. Montenegro, MD, PhD Douglas P. Olson, MD, FACP Department of Psychiatry, Yale University, New Haven, Connecticut. *Co-first authors

**Introduction:** Health disparities, having multifactorial causes, are systemic and pervasive. Health care providers have the capacity and, arguably, an obligation to alleviate the burden of health inequities on vulnerable populations. Accordingly, there is a need to adequately train health professional students to optimally practice in demographically diverse settings. We describe an 11-session course designed to provide students with practical skills and knowledge to address socioeconomic determinants of health in the clinical setting. The curriculum for this graduate-level seminar included workshops, readings, community outings, and reflection sessions.

**Methods:** This educational intervention study used survey data to assess changes in attitudes and skills among participants completing this course. This course was piloted using 25 randomly self-selected nursing, physician associate (PA) and medical students enrolled at a selective U.S. university. A 16-item instrument was developed to assess attitudes and skills that address socioeconomic determinants of health in the clinical setting. This survey was self-administered before and after the course. Responses were provided on a five-point Likert scale: 1 = “Completely Agree” to 5 = “Completely Disagree”. The data will be analyzed using STATA 11.0 (College Station, TX) statistical software. Somers’ D test and Fisher’s z-transformation will be used to perform both pre- and post-nonparametric comparisons of course participants’ pre-course responses to matched post-course responses. This study was approved by the University Institutional Review Board. Please note: Post-survey data is pending and will be available for analysis this upcoming week.

**Results:** A total of 21 students completed the course: 14 medical students, 2 PA students, and 5 nursing students. The mean age of the participants was 25 years old; 52% were male; 75% reported having parents with yearly household income greater than $60,000; and 62% self-identified as white students. Prior to completing this course, 100% of students strongly disagreed with the claim that “health disparities do not exist in the United States”; however only 44% agreed that they were confident with their ability to describe the causes of health disparities in America. Likewise, while 100% of students agreed that "socioeconomic factors account for the health disparities that exist in the United States”, only 15% agreed that they have the skills to address the environmental factors that influence a patient’s health.

**Conclusion:** All participants unanimously agreed that health disparities exist but fewer are able to describe causes. Implementation of this course will contribute to the training of students in becoming more socially conscious health care providers.
Understanding the Stories of "Super-Utilizer" Patients through Hotspotting on Tobacco Road: An Interprofessional Narrative-Based Approach to Reduce Rehospitalizations and Provide High Value Cost Conscious Care

Rita K. Kuwahara MIH, Melissa L. Cochran, Mark Dakkak, Stephanie Sun, Janelle Kwan, Kennetra Irby, Amy Weil MD

Introduction: According to the Agency for Healthcare Research and Quality, the top 1% of patients with multiple rehospitalizations—the "super-utilizers" of the healthcare system—account for 20% of the total $2.9 trillion spent annually on U.S. healthcare costs. These medically/socially complex individuals often have needs that substantially exceed the care available in clinical practice. To better understand factors contributing to these patients' use of healthcare, the objective of this study was to use the Association of American Medical Colleges (AAMC) method of "hotspotting" to collect the stories of "super-utilizer" patients in central North Carolina to develop individualized care plans that reduce rehospitalizations and improve health outcomes.

Methods: In this qualitative study, an interprofessional team of medical, social work, pharmacy, public policy, business, and divinity students at UNC-Chapel Hill and Duke University identified five "super-utilizer" patients with complex medical/social histories and recurrent hospitalizations to enroll and follow for 3-4 months. Team members collected patient narratives to examine underlying factors contributing to patients' health status/use of healthcare, conducted home visits, accompanied patients to clinic appointments, assisted patients with navigating the healthcare system, interviewed patients' providers, and reviewed the medical record. Enrolled patients had >3 hospitalizations in the past 12 months at UNC or Duke and >3 comorbidities. Patients under 18 years were excluded. Our project was funded through a hotspotting minigrant from the AAMC, Camden Coalition of Healthcare Providers, and Primary Care Progress, and was IRB exempt, as it was classified as quality improvement.

Results: All enrolled patients had multiple unmet social needs and >6 comorbidities, most commonly diabetes, heart failure, chronic pain, dental problems, and depression. Of the five patients, only two were retained throughout the study. Of the two patients, one had 10 hospitalizations in the past year with 34 inpatient days, and the other had 7 hospitalizations with 124 inpatient days. Both patients had stable housing, and one patient had strong social support. Both patients cited multiple system-level failures contributing to their hospitalizations, but neither was rehospitalized for the duration of the study, and information obtained from interviews was used to enable better navigation of the healthcare system, avoid previously encountered system-level failures, and improve care. The three patients lost to follow-up had less stable housing, a higher incidence of substance abuse, and were less likely to have a primary care physician.

Conclusion: Our findings highlight the importance of understanding patient narratives to develop interprofessional interventions that comprehensively manage clinical/social needs, reduce costs, and improve health outcomes. However, patients with significant social barriers in greatest need of narrative-informed care may be the most difficult to retain in interventions, and require novel approaches to achieve optimal health.
AGE- AND INFLAMMATION-RELATED ALTERATIONS IN RENIN ANGIOTENSIN SYSTEM MEDİATE BRAIN OXIDATİVE STRESS CHANGES

First Author: Sri Ramya Vajapeyajula Ambika Sharma, Joy Salib, Laura Powell, Ruth Marx-Rattner, Jeremy Walston, Peter Abadir

**Background:** Aging and chronic inflammation are major risk factors for neurodegenerative disorders. As the aging population is expanding, it is essential to investigate how the combination of aging and inflammation affects the progression of neuronal damage. One factor independently linked to both aging and inflammation is the Renin-Angiotensin System (RAS), but the effect of the combination of aging and inflammation on localized brain RAS and neuronal oxidative stress remains elusive. There is belief that oxidative stress resulting in cell damage serves as a prominent contribution to aging. A particular biomarker of oxidative stress, nitrotyrosine, is synthesized in both aging and healthy individuals at various levels. Elevation of the biomarkers has been previously witnessed within aging persons. We investigated the levels of angiotensin II type 1 receptor (AT1R) of the RAS pathway and its downstream effects on brain oxidative stress using mouse models of aging, inflammation and the combination of aging and inflammation. We aimed to determine if an association exists between RAS and oxidative stress that could potentially contribute to neurodegenerative disorders.

**Methods and Results:** Frontal cortex and cerebellar tissue from aged (100 wks. old); control and Losartan (LOS) (0.9 g/Liter in drinking water) treated, C57Bl6 and the mouse model of chronic inflammation (IL10^-/-), were isolated. Changes in the expression the angiotensin type1 receptor and its downstream effect on expression of Nitrotyrosine were analyzed using western blot. Our data suggest that AT1R levels were elevated in the cortex of IL10^-/- mice (1.54±0.54) compared to wild type (0.63±0.35 AU, p<0.0037). A similar increase in AT1R was also observed in cerebellar tissue (1.90±0.73 AU in C57bl6 vs. 4.14±2.26 AU in IL10^-/-). LOS treatment led to reduction in frontal cortex (p<0.04) and cerebellar (p<0.0534) AT1R. LOS treatment reduced protein level of Nitrotyrosine (p<0.0095) in the frontal cortex tissue and cerebellar tissue (p<0.06).

**Conclusion:** Aged IL10^-/- mice demonstrated elevated levels of AT1R in both the cerebral cortex and cerebellum tissues compared with wild-type mice. This was associated with elevated levels of Nitrotyrosine in both cerebellar and cortical tissue of IL10^-/- mice compared to wild-type. There was a significant reduction in AT1R and Nitrotyrosine levels in both areas of the brain when treated with LOS. Our data suggests a role for RAS in the pathogenesis of neurodegenerative disorders such as AD through increasing levels of oxidative damage. Angiotensin II receptor blockers such as Losartan could potentially serve as a therapeutic benefit in treating neurodegenerative disorders.
ONTARIO POSTER FINALIST - RESEARCH Priyanka Kapil

Implementation of fever advisory cards (FACs) as an initiative to improve febrile neutropenia management in a regional cancer center emergency department

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**Background:** Febrile neutropenia (FN) is a serious complication of chemotherapy with a mortality of up to 15%. The American Society of Clinical Oncology’s (ASCO) current guidelines for FN management support antibiotic administration within one hour of presentation to the emergency department (ED) to decrease adverse outcomes. Published reports suggest frequent delays in antibiotic initiation with mean times exceeding ASCO's guidelines. Many cancer centers utilize FACs as a tool for communication with patients and ED providers. No formal studies of the impact of FACs on quality exist. We aimed to assess the quality of FN management at a regional cancer center ED and assess the impact of the introduction of FACs.

**Methods:** Cancer patients who visited the ED at the Peel Regional Cancer Center in Ontario, Canada during pre-implementation (04/12 – 03/13) and post implementation (10/13 – 03/14) periods were identified. Patients were included if they received cytotoxic chemotherapy within 30 days prior to the ED visit, and if the presenting complaint to the ED was fever, infection or neutropenia. In the implementation phase all patients receiving cytotoxic chemotherapy received the FACs along with RN lead education. The primary outcome measure was the time to first dose of antibiotics. Process measures included the Canadian Triage and Acuity Score (CTAS), time to physician assessment in ED and use of the FACs. Outcomes were compared both with descriptive statistics and using statistical process control methods.

**Results:** 239 patients met inclusion criteria pre-implementation of FACs and 69 patients post-implementation. Post-implementation the mean time to antibiotics increased (194.7 min vs. 243.5 min, P = 0.09) and fewer patients received antibiotics within one hour (14.6% vs. 4.4%). Using statistical process control methodology, this was within normal variation. The percentage of correctly assigned CTAS scores increased (86.9% vs. 100.0%), but no significant change in mean time to physician assessment (97.3 min vs. 111.9 min, P=0.12) occurred. On follow-up assessment, only 65.2% of patients were carrying their FAC.

**Conclusions:** We identified a large margin for improvement in the management of cancer patients with suspected FN. The distribution of FACs did not demonstrate a meaningful or sustained improvement in the quality of FN management, however process assessment suggest inconsistent use of FACs may have contributed to the lack of improvement noted. Further process improvement targeting increased usage of FACs as well as ED assessment protocols are in development in an attempt to continue to work towards improved quality of FN care in our cancer patients.
Lysosomal Iron Modulates Synaptic Excitability via Dexras1/DMT1 Pathway in Neurons

Anup K. Bhattacharya, Rachel S. White, Yong Chen, Madeleine Byrd, Greg C. Carlson, and Sangwon F. Kim

Most of the studies of iron functionality in the brain have centered on its pathophysiological properties as a catalyst leading to the production of reactive oxygen species that contribute to neurodegeneration. Previously, we identified a novel signaling cascade in neurons whereby stimulation of glutamate-NMDA receptors activates small GTPase, Dexras1, inducing iron movement into the neurons via an iron channel, DMT1.

We demonstrated that Dexras1-mediated iron influx plays a crucial role in NMDA excitotoxicity. This also made us hypothesize that Dexras1-mediated iron influx may have a role in normal neurophysiological processes. Hence, we investigated whether disruption of NMDA-Dexras1-DMT1 cascades in neurons affects hippocampal activity and excitability.

We first confirmed that a pool of chelatable iron was rapidly generated at higher concentration in hippocampus CA1 area than in the dentate gyrus or CA3, and this change is dependent on NMDA receptor. We found that chelating iron with membrane permeable iron specific chelator, pyridoxal isonicotinoyl hydrazone (PIH) induced an increase in the frequency of spontaneous events (Control=0.9 +/- 0.09; 100µM PIH= 1.6 +/- 0.19Hz) and produced a 47% increase in evoked synaptic excitability. Also, iron chelation-mediated synaptic changes were abolished by DMT1 channel blocker or tissues prepared from Dexras1 knockout mice.

We further identified that iron is released via Dexras1/DMT1 pathway from lysosome. Importantly, when we disrupts lysosomal function, iron-mediated modulation of synaptic excitability is abolished. These data reveal a novel mechanism that demonstrates an active role of intracellular iron in modulating synaptic excitability.
I Am Men’s Health: Generating Adherence to HIV Pre-exposure Prophylaxis (PrEP) in Young Men of Color Who Have Sex with Men at 18 Months

First Author: Giffin W. Daughtridge, S. Caitlin Conyngham, Caroline E. Sloan, Karam Mounzer, and Helen C. Koenig

Background: Truvada (tenofovir/emtricitabine) is approved for pre-exposure prophylaxis (PrEP) for adults at risk of HIV and is highly effective at preventing HIV when taken daily. Young men of color who have sex with men (yMSMc) have the fastest growing incidence of HIV in the United States. However, no gold standard exists for consistently administering PrEP to this high-risk population. Our goal was to assess the effectiveness of a generalizable PrEP program that offers structured adherence support through weekly contact with yMSMc and individualized counseling to overcome barriers in a youth-friendly community setting.

Methods: These data reflect the first 72 weeks of an ongoing prospective observational study (February 2013 to August 2014). Most participants came on a weekly basis to pick up Truvada (n = 35), with 2 coming bi-weekly, and 4 coming monthly. Individual medication pick-up percentage was calculated for each participant for every six-week block that they completed since initiating PrEP. Those percentages were then averaged to determine the percent adherence for each reported interval.

Results: 41 participants (mean age 22.0, 73.2% African-American, 29.2% homeless or had insecure housing, 39% uninsured, 46.3% had Medicaid or Medicare) picked up PrEP for at least six weeks. Time on PrEP ranged from six to 76 weeks (13,440 person-days), as enrollment was rolling. Mean adherence for all participants was 57%, and the weighted average was 53%. Interval adherence was 79% for participants in their first six weeks (n=41), 46% from week 19 to 24 (n=33), 43% from week 31 to 36 (n=30), 33% from week 43 to 48 (n=22), and 61% from week 67 to 72 (n=3). Six prospective participants tested positive for HIV at their pre-program baseline screening and therefore were ineligible to join the program. 56% of participants tested positive for at least one sexually transmitted infection (STI) during the program: 20 cases of Gonorrhea detected by rectal swab, pharyngeal swab, or urine assay; 30 cases of Chlamydia detected by rectal swab or urine assay; 1 case of Trichomonas; and 1 case of Syphilis. 49% were non-immune to Hepatitis B at enrollment and were offered vaccination. No participants seroconverted to HIV.

Conclusions: The methodology used in this study generated an average adherence above 50% to PrEP over 72 weeks, although adherence varied over time. Despite six people being HIV+ at pre-program screening and diagnoses of STIs in 56% of participants, no HIV seroconversions occurred among this high-risk group of yMSMc. These findings provide useful information to inform large-scale HIV prevention interventions in the future.
**Hypothyroidism and pancreatic cancer: Role of exogenous thyroid hormone in tumor invasion.**

Shivam Saxena, Konrad Sarosiek, Ankit Gandhi, Christopher Kang, Galina Chipitsyna, Charles J. Yeo, Hvyda H. Arafat

**PURPOSE:** Assess the prevalence of hypothyroid patients receiving thyroid supplements in patients with pancreatic cancer and study how T4 influences cell behavior.

**METHODS:** A retrospective analysis was performed on patients who underwent a Whipple procedure from 2005-2012. The diagnosis of hypothyroidism was correlated with clinicopathologic parameters including tumor stage, grade, and survival. The functional impact of T4 on pancreatic cancer cell lines was studied using wound-induced migration, MTT proliferation assays, and invasion studies.

**RESULTS:** The prevalence of hypothyroidism in our patient population was 14.1%, compared to the 2-7% reported in the general elderly population. Hypothyroid patients were found to have higher rates of perineural invasion, nodal spread, and advanced prognostic stage (p<0.05). Cell line studies demonstrated that exogenous T4 increased cell proliferation, migration, and invasion (p<0.05).

**CONCLUSIONS:** Exogenous thyroid hormone may contribute to tumor aggression in pancreatic cancer.
Effect of Statins on the mortality of bacteremic patients: A Systematic Review and Meta-analysis of clinical trials

First Author: Pragya Shrestha, MBBS Co-authors: Dilli Ram Poudel MD, Ranjan Pathak MD, Sushil Ghimire MD, Madan Raj Aryal MD, Paras Karmacharya MD

BACKGROUND: The pleiotropic effects of statins have been shown to modify inflammatory cell signaling during the immune response to infection. It has been postulated that statins could halt endothelial apoptosis, decrease isoprenylated proteins necessary for leukocyte cellular signaling, modulate endothelial cell adhesion molecules, proinflammatory cytokines and regulate chemotactic proteins. Studies in the past have shown inconsistent results with some studies suggesting beneficial effects of statins in inflammatory conditions such as bacteremia, pneumonia and sepsis; and others showing potential harm. We therefore sought to perform a systematic review and meta-analysis on the effect of statins on the mortality of bacteremic patients.

METHODS: Relevant studies were identified through MEDLINE, EMBASE, Cochrane Library, Scopus and clinicaltrials.gov electronic databases, and hand-search from inception through December 2014. Prospective and retrospective observational cohort studies examining the association between statin use (on hospital admission or previous users) and the outcomes of bacteremic patients were included. The outcome of interest was overall hospital mortality at the longest follow up at each single study. The statistical analysis was performed using RevMan5.2 software. A P-value of <0.05 was considered statistically significant. Study specific risk ratios were calculated and combined using random-effects model meta-analysis. Between studies heterogeneity was assessed using the I² statistics. Quality assessment of included studies was performed using the Newcastle-Ottawa Scale.

RESULTS: Six cohort studies comprising 7,553 patients were eligible. The overall hospital mortality was 15.36% (139/905) in patients on statin versus 22.28 % (1481/6648) in patients not on a statin (OR 0.49; 95% CI 0.30-0.81, I² = 69%, p= 0.005). Quality analysis showed that all the included studies were of high or moderate quality (16.67% high and 83.33% moderate scores).

CONCLUSION: Our study showed that statin treatment in bacteremic patients was associated with significantly lower mortality rates and there may be a potential role for statins in similar inflammatory conditions. The optimum dose and type of statin (hydrophilic vs. lipophilic) and the mechanism by which statins potentially halt the inflammatory cascade remains an area of further study. Large, well designed randomized controlled trials are warranted to provide more conclusive knowledge and potentially change clinical practice.
Autotaxin is an Independent Predictor of Insulin Resistance in Overweight and Obese Females

First Author: Joy Siting Trybula, PharmD Valerie L Reeves, PhD Erin E Kershaw, MD

Introduction: Worldwide obesity has nearly doubled since 1980 and prevalence of insulin resistance has increased concurrently. Obesity is associated with the dysregulation of adipokines, which are adipose tissue secreted hormones that influence metabolism. A novel adipokine, autotaxin (ATX), hydrolyzes lysophosphatidylcholine (LPC) to generate lysophosphatidic acid (LPA) – a lipid signaling molecule. In vitro studies implicate the ATX-LPA pathway in the development of insulin resistance, however the mechanism and relationship remains unknown. We hypothesize that there is a positive association between serum autotaxin and features of insulin resistance in humans.

Methods: The current study was completed using previously collected samples from the Re-Energize with Nutrition, Exercise, and Weight loss study (RENEW). The RENEW trial was designed to determine the efficacy of diet, exercise, and combination diet and exercise on weight loss in the obese. We assessed middle-aged, non-diabetic, overweight to obese female subjects for markers of insulin sensitivity, inflammation, and features of metabolic syndrome. Baseline serum ATX was measured by ELISA and data were analyzed using Spearman’s correlation test. Multivariate stepwise linear regression was used to determine predictive value of serum ATX.

Results: Serum ATX concentrations from 208 female subjects were evaluated. Median (IQR) age and BMI were 47.2 (40.6-51.9) years and 36.8 (27.3-43.2) kg/m2, respectively. As predicted, serum ATX concentration was higher in overweight to obese females (277.6 ng/mL) compared to normal weight females (211.4 ng/mL, p<0.0001). ATX correlated with insulin resistance in overweight to obese females (rho=0.3871, p<0.0001) and was independently associated with homeostatic model assessment of insulin resistance (HOMA-IR) (Multivariate OR [95%CI]) (0.002 [0.001-0.004], p=0.007).

Conclusion: Serum ATX is positively correlated with HOMA-IR and, more significantly, is an independent predictor of insulin resistance in our cohort. Serum ATX may be used as a therapeutic target or as a clinical diagnostic parameter for insulin resistance and diabetes.
RHODE ISLAND POSTER FINALIST - RESEARCH Caitlin Naureckas

Bridging the Geographic Divide: Feasibility and Outcomes of GeneXpert Screening in Smear-Negative Tuberculosis Suspects in Western Kenya

First Author: Caitlin Naureckas Additional Authors: B Pederson MD, R Boinett, J Jezmir, L Kamle, N Buziba MBChB, A Gardner MD, MPH, W Injera, MBChB, EJ Carter MD

Background: Tuberculosis (TB) remains a major global health burden, with an estimated 8.7 million new cases in 2011. Sputum smear microscopy is inexpensive and the most widely-used diagnostic in resource-limited countries, but is limited by its low sensitivity, especially in patients co-infected with HIV. Diagnosis of MDR TB traditionally relies on drug-susceptibility testing of cultured samples, which is costly and time-consuming. The GeneXpert MTB/RIF is an automated, cartridge-based test that uses real-time PCR for diagnosis of active TB infection and detection of rifampin resistance.

Methods: We designed a proof-of-concept intervention to determine whether the diagnostic advantages of GeneXpert could be extended to smear-negative TB patients living out of range of large referral hospitals. A “hub and spoke” model was implemented, placing Xpert machines at three “hub” clinic sites in Western Kenya and selecting an additional 29 “satellite” clinics to send patient sputa for screening on the central machines. In January 2012, Xpert testing was initiated on sputum samples of patients who met the Kenyan Division of Leprosy, TB, and Lung Disease (DLTLD) definition of a smear-negative TB suspect: smear-negative spot and morning sputum sample. Original sputa were transported from the satellite sites twice a week via motorbike and run on Xpert within 72 hours of collection.

Results: Overall, 1439/2407 (59.8%) of smear-negative suspects at study sites received GeneXpert testing; 1387 (96.4%) received definitive Xpert results. The percentage of patients with two sputum samples collected and screened via Xpert started at 23.3% in the first quarter and rose to 77.9% in the fourth quarter. 122 (8.8%) of the smear negative patients tested were confirmed by Xpert to have TB. 2 (0.1%) patients were found to have rifampin-resistant infection. Patients diagnosed with pulmonary TB with rifampin resistance by Xpert were immediately started on second line treatment at the original site per DLTLD guidelines. Those who were MTB+ without rifampin resistance were started on first-line TB treatment.

Conclusion: Our results demonstrate that GeneXpert can be feasibly placed and operated in peripheral health care units in the developing world to supply rapid microbiologic diagnoses of TB to patients geographically distant from central laboratories. 91.1% of tested patients received a negative GeneXpert test, which allowed for further evaluation of alternate diagnoses rather than blind enrollment onto TB treatment. As sample quality was a major cause of error results, further training of clinicians and patients in best sputa collection methods can increase the number of patients receiving a definitive result.
Rhode Island Poster Finalist - Research Joshua Rodriguez-Srednicki

Understanding Patient Perceptions of Resident Well-Being and Transfers of Care

Joshua Rodriguez-Srednicki, Brian C. Drolet; Charles H. Hyman; Kimeya F. Ghaderi; Jordan M. Thompson; Staci Fischer

Background: Duty hour reform has focused on the association between resident fatigue and medical errors. Pressure from the public and the Institute of Medicine to further restrict duty hours and increase supervision of residents continues to shape residency training in the U.S, which must comply with the 2011 Accreditation Council for Graduate Medical Education (ACGME) Common Program Requirements.

Objectives: Despite strong public impetus, there has been little patient engagement in revision of duty hour regulations. To address this gap, we sought to produce the first cross-sectional study of patient perceptions from a large and diverse sample of hospitalized patients regarding the impact of duty hour regulations on continuity of care and patient safety following implementation of the 2011 Common Program Requirements.

Methods: A 32-question instrument was designed, and following Institutional Review Board approval, we sampled patients at both Rhode Island and Miriam Hospital between June and August 2013. All adult inpatients under the care of a resident team were eligible for inclusion. Patients without decision-making capacity were excluded. Significant differences were established using one-sample hypothesis tests of a multinomial distribution.

Results: A total of 513 surveys were obtained from 810 patients (63.3% response rate). Most patients believed that average resident shifts were no longer than 16 hours (78.2%) and that residents should not be assigned to shifts longer than 12 hours (57.1%). Nearly half of patients (49.7%) wanted to be notified if a resident had worked longer than 12 hours. More than 60% felt that medical errors occur commonly due to fatigue, and that further reducing work hours would reduce medical errors (61.5%). Notably, 67.8% reported that the residents caring for them did not seem fatigued. While 64.1% of patients believe that important information can be lost during transfers, only 21.1% felt less confident after a hand-off, and only 37.5% (OR 0.56, p<0.01) believed that medical errors were commonly due to transfers of care. Finally, given the choice between “a familiar doctor, who may be fatigued at the end of a long shift,” and “an unfamiliar doctor, who is just starting a shift and has received sign-out,” significantly more patients chose the unfamiliar “fresh” doctor (57.2% vs. 42.8%, p<0.01).

Discussion: While patients reported concerns about the potential risk of medical errors from resident fatigue, they noted less worry over risks from transition of care. Although fatigue mitigation is important, many program directors and residents have expressed concerns that duty hour restrictions have resulted in more transitions of care, inadvertently leading to errors and compromising resident learning. This study demonstrates a gap between patient and physician perceptions of duty hour regulations and highlights an opportunity to foster further public education, empowering patients to meaningfully contribute to public discourse on residency training.
SAUDI ARABIA POSTER FINALIST - RESEARCH Abdullah Talat Eissa Sr

Antimicrobial Dosing Errors in Critically Ill Patients

First Author: Abdullah Talat Eissa Sr Dr. Hasan Al-Dorzi ICU consultant

Introduction: Severe sepsis occurs at the rate of three cases per 1000 population in the United States leading to 750,000 sepsis patients per year with a mortality of 28.6% (1). A retrospective chart review of 1044 patients >80 years admitted to the University of California, and all prescribed antibiotics were identified and studied. Dosing errors were found in 34% of prescribed antibiotics (2). Hence dosing errors of antimicrobial agents are common, they can be harmful. Furthermore, they are likely to be more profound in high risk patients such as the critically ill. The aim of the study is to study the frequency and the risk factors of antimicrobial dosing errors in adult critically ill patients at Intensive Care Department (ICU) at King Abdulaziz Medical City KAMC.

Methodology: This is a prospective cross-sectional observational study of all adult patients admitted under ICU service during six consecutive months. Doses of ordered antibiotics were compared against the recommended doses as per Micromedex. The margin of error was 5% with confidence level 95% and 20% response distribution of estimated population of 800. The calculated minimum required sample size came out as 189 patients. 200 patients were included to account from any missing data. Each patient was evaluated daily during ICU stay for 7 days. Creatinine clearance was calculated according to the Cockcroft and Gault equation, and Liver function was assessed using Child Pugh score. Analysis was done by using SPSS statistical software. Chi Square test and student t-test were used to compare between the variables. Multivariate logistic regression analysis was done to assess the predictors of antimicrobial dosing errors.

Results: Of 200 evaluated patients, 189 were eligible and hence included in the study. Out of 189 patients in the study, 117 (61.9%) received appropriate antimicrobial doses. Nevertheless, 30 (15.9%) patients had antibiotic under-dosing, 39 (20.6%) over-dosing, and 3 (1.6%) combination of over-dosing and under-dosing. Most of septic shock patients (77.9%) had antimicrobial dosing errors compared with 22.1% of patients with severe sepsis (P=0.001). Furthermore, Septic patients with cardiovascular and renal insufficiency were more likely to have antimicrobial dosing error (P=0.035) and (P=0.021), respectively. On the other hand, respiratory failure, liver failure, immunodeficiency and diabetes mellitus were not associated with dosing error. Regarding the multivariate analysis, GFR was the only variable that was associated with dosing error. Piperclillin/tazobactam was the most commonly prescribed antibiotics. More than 20% of the patients who received meropenem did not have appropriate antimicrobial dosing. More than 70% of patients who received imipenem, ciprofloxacin and gentamicin had the appropriate antimicrobial doses. In addition, 93.8% of patients on Ceftriaxone had correct doses. However, Vancomycin was associated with the lowest rate of appropriate dosing with 57.4%. Colistin was the only medication which was prescribed with 100% appropriate doses.

Conclusion: 117 (61.9%) of the samples had accepted antimicrobial doses. In regarding to some characteristics and comorbidities, the study shows that cardiovascular comorbidities, renal insufficiency and patients were diagnosed with septic shock have higher tendency to have antimicrobial dosing errors. In the matter of antimicrobial use, Vancomycin had the highest rate of inappropriate dosing with 42.6%. Patients who received Tazocin, Meropenem, Imipenem, Ciprofloxacin and Gentamicin gained success rate of 70%. Moreover, 93.8% of Ceftriaxone doses were suitable, and all of the colistin doses were appropriate.

First Author: Katrin Eurich Meagan Keefe, Ali Seifi MD, FACP

Introduction: Acute myocardial infarction (AMI) is the leading cause of morbidity and mortality in developed countries, according to the World Health Organization. The purpose of this study is to determine the impact of teaching versus non-teaching institutions on the AMI mortality rate in the United States from 2000 to 2011 using a robust database.

Methods: This is a retrospective cohort study of AMI mortality rates in the United States during 2000-2011. Data from the Nationwide Inpatient Sample (NIS) was queried for inpatient admissions with a primary diagnosis of AMI using the Agency for Healthcare Research and Quality (AHRQ) Quality Indicators (QI). Mortality rates were adjusted by patient and hospital characteristics, and Z-tests were performed using statistical analysis. All statistical testing was 2-sided with a Bonferroni correction for multiple comparisons and a nominal 5% significance level.

Results: The incidence of AMI mortality significantly decreased during the study period, from 102.364 in 2000 to 48.656 deaths per 1,000 hospital admissions in 2011 (p < 0.01). Mortality was significantly higher in females than in males (p < 0.01) and was significantly higher in the 65+ age group than in all younger age groups (p < 0.01). By income, mortality was significantly higher in the lower two quarters than in the highest quarter for all years of this study excluding 2011 (p < 0.01). Teaching institutions had significantly lower mortality rates for AMI than non-teaching institutions in each year (p < 0.05). Mortality per 1,000 hospital admissions at the beginning of the study was 95.39 at teaching institutions and 105.378 at non-teaching institutions. In 2011, mortality rates declined to 47.574 at teaching institutions, significantly less than the mortality rate of 49.227 at non-teaching institutions (p < 0.01).

Conclusion: Our data shows that AMI is a common cause of death in the United States, and mortality rates have steadily declined from 2000 to 2011 across all institutions. Treatment of AMI at teaching institutions results in significantly lower mortality rates than does treatment at non-teaching institutions during all years of the study period. This could relate to a higher level of care provided in teaching institutions. Further studies are needed to determine the factors contributing to this difference in an effort to further reduce AMI mortality rates in the United States.

References:

Is There a Causal Relation Between Maternal Acetaminophen Administration and ADHD?

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Objective: Recent studies show an association between maternal intake of acetaminophen (APAP) and attention deficit hyperactivity disorder (ADHD) in their children. However, none of these studies have experimentally addressed causality. Our objective was to determine the causal relationship between prenatal APAP exposure and phenotypic characteristics of ADHD in a murine model.

Study Design: Pregnant CD1 mice (N=8/group) were allocated to receive by gavage either APAP (150 mg/kg/day, equivalent to the FDA-approved maximum clinical dose), or 0.5% carboxymethylcellulose (control group), starting on embryonic day 7 until delivery. Maternal serum APAP and alanine transaminase (ALT) concentrations were determined by ELISA and kinetic colorimetric assays, respectively. Open field locomotor activity (LMA) in the 30-day old offspring was quantified using Photobeam Activity System. Offspring were then sacrificed, whole brains processed for resonance imaging (MRI; 11.7 Tesla magnet) and for neuronal quantification using Nissl stain. The association between APAP exposure and LMA in offspring was analyzed using a mixed effects Poisson regression model that accounted for offspring weight, gender, random selection, and testing time and day; P<0.008 (corrected for multiple testing) was considered significant.

Results: The maternal serum concentration of APAP peaked at 30 min after gavage, reaching the expected mean of 117 μg/ml. Serum ALT levels were not different between groups. There were no significant differences in vertical (rearing) or horizontal activity between the two offspring groups at the P level fixed to adjust for multiple testing. In addition, no differences were found in volumes of 30 brain areas of interest on MRI or in neuronal quantifications between the two groups.

Conclusion: This is the first study assessing the causality of APAP prenatal exposure and risk of ADHD. Our preliminary results do not support a causal relationship. Results of epidemiological studies are likely due to confounding factors that were unaccounted for.
A Year of Infection in the ICU: prospective whole genome sequencing of all ICU clinical bacterial isolates reveals hidden outbreaks and novel pathogens within a hospital environment

First Author: David Roach Joshua Burton, Choli Lee, Jay Shendure, and Stephen J. Salipante

Introduction: In the United States, healthcare-associated bacterial infections affect approximately 2 million patients annually and result in nearly 100,000 deaths. To better understand the pathogenesis and transmission of bacterial pathogens, it will be necessary to employ comprehensive analytic approaches able to biologically characterize the organisms and to reconstruct their molecular epidemiology. Whole genome sequencing (WGS) is emerging as a powerful method for these types of analyses, but is not yet used in routine clinical care. WGS studies to date have typically been limited in that they have been 1) retrospective in nature, 2) limited in scope to particular bacterial species, and 3) extended to subsets of bacterial isolates, rather than globally across an entire patient population. Here, we performed prospective collection and WGS of all bacterial isolates collected from three intensive care units within a single hospital over a period of one year. This enabled us to examine many aspects of organisms infecting our patient population, including the identification of previously unreported pathogens and large-scale, longitudinal reconstruction of bacterial transmission events.

Methods: We sequenced 1,260 clinical isolates collected during routine care across three intensive care units over a 12-month period at the University of Washington Medical Center. After assembly, genomes were BLASTed against NCBI databases to establish their identity, and sequence divergence was quantified with Average Nucleotide Identity by BLAST (ANId) to identify new species (defined as ANId value <95%). Finally, a single nucleotide variant analysis was performed to unambiguously identify instances of clonal bacteria found between patients.

Results: 35.2% (445/1262) of bacterial isolates qualified as new species at the genomic level. 77 distinct “species clusters” were identified, with 51 consisting entirely of unknown species while 26 were a mixture of known and novel species. New species were isolated from all anatomic culture sites and consisted of both commensal and pathogenic isolates. There were 116 instances of clonal bacteria found across multiple patients, representing likely bacterial transmission events. 8 different species were involved. 11 separate Staphylococcus epidermidis strains were found across multiple patients, including 3 strains found exclusively in the neonatal intensive care unit (NICU). All of these isolates were associated with intubated infants, and one strain caused sepsis in 5/9 infants from whom it was cultured.

Conclusions: We found a surprisingly high prevalence of new bacterial species infecting ICU patients, many of which are related to known species but some representing entirely novel pathogens whose clinical and biological significance remain unexplored. Additionally, we identified cryptic outbreaks not recognized by hospital infection-control teams, most notably within the NICU. This study demonstrates the power of using WGS routinely in the clinical management of infectious disease, both for improving infection-control practices and for expanding our understanding of bacterial pathogens.
Targeting NADPH-Mediated Oxidative Stress Reduces Cell Death and Improves Behavior following Neurotrauma


1.7 million traumatic brain injuries (TBIs) occur each year in the United States. Recent evidence suggests that repetitive TBIs can lead to chronic neurodegenerative changes over time. Currently, available pharmacologic options for the treatment of acute neurotrauma are limited. Oxidative stress is an important secondary mechanism of injury that can lead to cellular apoptosis and behavioral changes such as impulsivity. Utilizing a clinically relevant and validated rodent blast model, we investigated how NADPH oxidase expression and associated oxidative stress contributes to cellular apoptosis following single and repeat blast injuries.

Nox4 forms a complex with p22phox following injury, both of which are important subunits of the NADPH oxidase system found within the brain. Using immunohistochemical-staining methods, we found a visible increase in Nox4 following single blast injury in Sprague Dawley rats. Interestingly, Nox4 was also increased in post-mortem human samples obtained from athletes diagnosed with chronic traumatic encephalopathy (CTE). Nox4 activity correlated with an increase in superoxide formation. Alpha lipoic acid, an oxidative stress inhibitor, prevented the development of superoxide acutely, and increased anti-apoptotic markers Bcl-2 ($t=3.079, p<0.05$) and heme oxygenase 1 ($t=8.169, p<0.001$) after single blast exposure. Subacutely, alpha lipoic acid treatment reduced pro-apoptotic markers Bax ($t=4.483, p<0.05$), caspase 12 ($t=6.157, p<0.001$), and caspase 3 ($t=4.573, p<0.01$) following repetitive blast, and reduced tau hyperphosphorylation indicated by decreased CP-13 and PHF staining.

Alpha lipoic acid ameliorated impulsive-like behavior 7 days after repetitive blast injury ($t=3.573, p<0.05$) compared to blast exposed animals without treatment. TBI can cause debilitating symptoms, disability, and psychiatric disorders. Secondary mechanisms of injury, such as oxidative stress, are ideal targets for neuropharmacologic intervention. Alpha lipoic acid warrants further investigation as a therapeutic for the treatment of acute neurotrauma and prevention of chronic neurodegeneration.
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