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PRETENDING TO BE THE GREAT PRETENDER

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Introduction: The *Treponema pallidum* species of bacteria has been called “*Treponema pretendium*” for its ability to mimic other infectious and non-infectious diseases. The *Treponema* genus has at least four subspecies that cause disease in humans. Infection by spirochetes continue to be a preventable cause of morbidity and mortality worldwide. Of the *Treponema pallidum* species, most familiar is *Treponema pallidum pallidum*, the spirochete known to cause syphilis. The other *Treponema pallidum* subspecies continue to be diagnostic challenges.

Case: A 46 year-old male visiting from Ghana presented with a three day history of itching papules. The patient reported malaise, diffuse myalgias, and feeling febrile prior to the cutaneous papular eruption. The papules began on his face and spread caudally. He has no recent medical or family history, no known allergies, and is not taking medications. The sexual history revealed no recent history of genital chancre and no recent new sexual partners.

On physical examination, his vital signs were normal. The skin exam revealed diffuse 2-5mm flesh colored papules and papules coalesced into plaques on the face. There was no palmar, plantar, or genital involvement. Examination of the lymph nodes and oral mucosa showed no significant findings. The neurological exam was similarly unremarkable.

A number of etiologies were initially suspected, including viral exanthem, HIV-associated folliculitis, and secondary syphilis. Lab results showed a negative HIV antigen test; however, the RPR was reactive with a 1:4 titer. The confirmatory FT-ABS test was also positive.

His presentation was consistent with yaws. He was treated with 2 grams of azithromycin, as recommended in recent literature, and reported feeling well after treatment. On two week follow up the lesions resolved, leaving only mild scarring and post-inflammatory hyperpigmentation. No Herxheimer reaction to the antibiotic was reported.

Discussion: Yaws is a treponemal infection that is contagious through non-sexual skin contact. Left untreated, yaws can cause disfiguring skin lesions and bone, cartilage, and soft tissue destruction. It should be suspected in patients from endemic countries such as Ghana, Cote d'Ivoire, and Papua New Guinea. There is a current World Health Initiative to eradicate yaws worldwide; this program has successfully eradicated Yaws in India.

By recognizing the presentations and endemic areas of yaws, a healthcare professional can help eradicate this highly transmissible and potentially disfiguring treponemal disease that has a low cost of treatment and high cost if left untreated.

PREGNANCY IN SIMULTANEOUS PANCREAS-KIDNEY (SPK) TRANSPLANT: IS IT WORTH THE RISK?

Francis Tinney Jr, Taneev Escamilla, Rohini Prashar MD, Mariella Ortigosa-Goggins MD, Jerry Yee MD

Introduction: While numerous successful pregnancies in recipients of solid organ transplants have been reported, definitive data on maternal, fetal and graft outcomes is still lacking. We report an interesting case of renal allograft rejection that occurred in a simultaneous pancreas and kidney (SPK) transplant recipient during pregnancy.

Case: We describe a renal graft rejection without pancreatic graft rejection in the third trimester of a previously normal pregnancy in a SPK transplant recipient. A 36-year-old woman with end-stage renal disease, secondary to type 1 diabetes mellitus, had received a SPK transplant four years prior to a planned pregnancy. Two months before pregnancy, mycophenolate mofetil was substituted for azathioprine. Gestation was uneventful until week 32 weeks when the patient developed an acute elevation of serum creatinine (SCr) from 0.8 mg/dL to 3.6 mg/dL, worsening hypertension, and sub-therapeutic tacrolimus level (2.2 ng/ dl). The concern for potential allograft failure prompted urgent induction of labor, in order to conduct a kidney biopsy and modify the immunosuppression regimen. A postpartum renal biopsy demonstrated acute renal graft cellular rejection (Banff 1B). Subsequent treatment with five doses of thymoglobulin led to a decline in SCr to 2.1mg/dL.

Discussion: The National Pregnancy Transplant Registry does not report an increased risk of rejection during pregnancy in kidney-only transplant recipients. Still, there is a paucity of data for graft outcomes in SPK transplant recipients. Our case highlights the high-risk graft rejection period in pregnancy and postpartum. In addition, this case underscores the importance of scrupulous monitoring of tacrolimus levels during pregnancy.

JEJUNAL VARICES: A RARE SOURCE OF GASTROINTESTINAL BLEED

First Author: Ankita Satpute, Medical Student, Case Western Reserve University School of Medicine, Cleveland, OH

Introduction: Esophageal (50%), gastric (5-33%), and rectal varices have been identified as the most common sites of gastrointestinal varices in patients with portal hypertension. While varices may develop anywhere along the GI tract, suspicion for jejunal varices is often low and they can be difficult to diagnose. This case is one of few documented reports of enlarged jejunal varices as an isolated source of GI bleed.

Case Presentation: A 64-year-old Caucasian male with a history of Factor V Leiden Mutation and recurrent DVTs/PEs presented to an outside ED with a one week history of shortness of breath and lightheadedness along with a one day history of tarry black stools.

In concordance with his symptoms, the patient was found to have severe anemia with a hemoglobin level of 5.9 and was subsequently transfused multiple units of packed RBCs. Chest CTA confirmed bilateral pulmonary embolisms. Following diagnosis, the patient was stabilized and transferred to main campus for anticoagulation in the setting of a GI bleed.

The patient was admitted to main campus in stable condition and received further blood transfusions after additional episodes of melena and endorsement of orthostatic hypotension. The Gastroenterology team investigated the source of bleeding through multiple diagnostic procedures including EGDs, colonoscopies, and push enteroscopy, which were all negative for a likely source. Ultimately, a double balloon enteroscopy was successful in identifying isolated and enlarged jejunal varices (>5mm) in two areas of the jejunum as the source of bleeding. These varices were not amenable to endoscopic intervention, but were repeatedly monitored throughout the hospital course. Of note, no esophageal varices were documented, and otherwise, only isolated type II gastric varices were visualized, but were not considered significant in the setting.

Portal hypertension in this patient was manifested secondary to chronic portal vein and superior mesenteric vein thromboses, with no evidence of liver cirrhosis. The patient underwent successful surgical intervention to construct a side-to-side variceal caval anastomosis with a portosystemic shunt and placement of an IVC filter. After a challenging recovery, the patient was discharged home in stable condition with an emphasized need for life-long anticoagulation.

Discussion: This case highlights the importance of visualizing the small bowel and investigating jejunal varices as a potential source of gastrointestinal bleeding in patients with portal hypertension. In this unique report, large jejunal varices were identified as the etiology of GI bleed without evidence of esophageal varices and only visualization of nonbleeding type II gastric varices. Double balloon enteroscopy is a challenging procedure, but may be effective in investigating the small bowel when other sources of GI bleeding have been negated.

THE TRUTH IS IN THE SMEAR

First Author: Nainesh Shah, MD Second Author: Kartik Rajagopalan, PhD

Case Presentation A 34-year-old Liberian woman with a history of HIV and AIDS diagnosed 10 years prior had not been taking anti-retroviral therapy for the past four years when she presented with two weeks of fever, frontal headache, vomiting, right upper quadrant abdominal pain, and non-productive cough. When she arrived, she had a temperature of 40 degrees Celsius, tachycardia to 110 beats per minute, and a normal respiratory rate and oxygen saturation. She was in mild discomfort and diaphoretic. Her physical examination demonstrated mild epigastric tenderness without rebound or guarding but was otherwise unremarkable.

Her laboratory workup revealed a CD4 count of less than ten, elevated transaminases and alkaline phosphatase (AST=189, ALT=39, Alkaline Phosphatase = 164), and normal bilirubin levels. She had a white blood count of 1650/microliter with a normal differential, hemoglobin of 10.5 g/dL, and platelet count of 28,000/microliter. Abdominal ultrasound and computed tomography (CT) showed diffusely enlarged abdominal lymph nodes. Chest CT showed evidence of healed calcified granulomas and non-specific mildly enlarged mediastinal lymphadenopathy. MRI of her brain was unremarkable. Lumbar puncture was performed and CSF analysis showed less than 1 nucleated cell/microliter with normal glucose and normal protein. Toxoplasma IgG was negative and serum analysis for CMV showed 2,460 DNA copies/mL. She was started on Vancomycin and Zosyn.

She continued to have high fevers intermittently to 40 degrees Celsius. Her ferritin level and lactate dehydrogenase were both elevated to greater than 100,000 ng/milliliter and greater than 2133 units/liter respectively. Her blood smear was referred to the pathologist who noted intracellular yeast. A presumptive diagnosis of disseminated histoplasmosis was made and she was started on AmBisome. Urine Histoplasma antigen later detected greater than 20 ng/mL and fungal blood culture eventually grew Histoplasma capsulatum.

Discussion Disseminated histoplasmosis occurs when spores are inhaled into the lungs and transform to yeast which are able to travel through the blood stream. It is a common opportunistic infection in the AIDS population, but the diagnosis is often delayed because the urine antigen test is a send-out study that takes several days to return. In this case, the patient's blood smear aided in the diagnosis and initiation of appropriate therapy.

Conclusions The incidence of Histoplasma detection on peripheral blood smear is not well quantified and is likely under-reported. A blood smear is relatively inexpensive and results can be obtained immediately. This low cost and high yield test would assist in a quicker diagnosis and prompt initiation of therapy sooner. Internists should consider routinely engaging the pathologist in reviewing the blood smear when disseminated histoplasmosis is in the differential.

INSULIN UNDER DURESS-IDENTIFYING AND TREATING INSULIN AUTOIMMUNE SYNDROME

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Case: A 79-year-old Caucasian non-diabetic male with history of renal cell carcinoma, s/p left nephrectomy in 2005 and coronary artery stent placement 2 months prior and on Clopidogrel, presented with acute onset sweating and palpitations. Monitoring revealed fasting serum glucose as low as 29mg/dL with concurrent insulin level of 9,600 uIU/mL. Further investigations for the cause of his hyperinsulinemic hypoglycemia showed a C-Peptide of 18.9ng/mL ruling out exogenous insulin, a negative sulfonylurea screen, negative anti-islet cell antibodies and Chromogranin A of 24ng/mL suggesting a neuroendocrine tumor. A work up for Insulinoma included an MRI of the Pancreas and EUS both of which came back negative. Given the negative Insulinoma work-up and such uncharacteristically high Insulin levels, a Paraneoplastic syndrome with ectopic Insulin secretion versus a drug-induced autoimmune process was considered. A negative whole body PET/CT ruled out a paraneoplastic process but the anti-Insulin antibody titer was high (11 nmol/L, range 0.00-0.02) confirming the diagnosis of Insulin Autoimmune Syndrome

The patient was started on Diazoxide 80mg TID and Dexamethasone 2mg BID on day 10. Serum glucose ranged from 50-80mg/dL to >350 mg/dL post-prandial. Clopidogrel was determined to be a possible inciting cause and was replaced on day 18 with Tacagrelor. Total serum insulin then measured was 20,900uIU/mL with a normal free insulin level. With no further hypoglycemic episodes the patient was discharged on the above treatment on day 22 with Endocrine follow-up.

Discussion: Insulin Autoimmune Syndrome (IAS) is described as spontaneous hypoglycemia due to insulin autoantibodies in the absence of exogenous insulin. IAS is a leading cause of hypoglycemia in Japan but is rarely diagnosed in the US. Diagnosing and treating IAS can be straightforward, and knowledge of this disorder may eliminate unnecessary procedures and delay in treatment.

This case illustrates the need to consider drug-induced IAS in patients with acute onset hyperinsulinemic hypoglycemia and no history of exogenous insulin exposure. In IAS antibody-bound serum insulin builds and is released erratically resulting in extreme hypoglycemia. Literature review suggests that medications with a sulfhydryl group are known to trigger IAS particularly in patients who are positive for the HLA-DRB1 gene. The most common offending drug is alpha-lipoic acid, with Methimazole, Glutathione, Imipenem, and Hydralazine also implicated. Stopping the suspected drug typically reverses IAS. Our patient tested positive for HLA-DRB1-04:04 and all his medications including OTC supplements were reviewed. Clopidogrel, whose active metabolite contains a sulfahydryl group, was felt to be the offending agent and was discontinued. He has had no episodes of hypoglycemia since discharge.

STUDENT CLINICAL VIGNETTE POSTER FINALISTS

CARCINOID TUMOR AND CARDIAC MASS: REPORT OF AN UNUSUAL CASE

Karli Singer, BS, MS IV, Suzanne Sorof, MD, William Peppo, DO

Introduction: Cardiac tumors are extremely rare, but have potentially life threatening consequences as the mass can lead to embolic events or interfere with valvular function. They can be asymptomatic and found incidentally while screening for other disorders. We present an unusual case as an example of how they may be discovered.

Case Description: A 64-year-old male with uncontrolled hypertension saw his primary care provider for his annual physical. He was asymptomatic and his physical exam was unremarkable. A screening colonoscopy was performed which revealed a rectal mass. A biopsy confirmed it to be a carcinoid tumor. The patient underwent further workup and staging of the carcinoid tumor. Incidentally, a partially calcified 1.5 x 2.1 cm mass arising from the left atrial septum was identified on chest CT scan. A transesophageal echocardiogram was performed to evaluate the cardiac mass. A 1.54 x 2.0 cm calcified sessile neoplasm was attached to the middle of the left atrial septum. This was thought to be a cardiac myxoma. There were no clots noted in the atrial appendage. To assess his cardiac function, a cardiac catheterization was completed which showed a 50-60% stenosis of the right coronary artery (RCA). The patient was referred to a cardiothoracic surgeon who resected the tumor and removed the atrial septum, replacing it with a graft. A CABG x1 to the RCA was also performed. He did well postoperatively and was discharged home after four days.

The tumor was sent to pathology for histologic classification. No typical histologic features of myxoma were identified, but in fact a cardiac calcified amorphous tumor (CAT) was described. The patient is currently doing well and his hypertension is well controlled. He is following up with cardiology and cardiothoracic surgery for the cardiac mass and oncology for his carcinoid tumor.

Discussion: Calcified amorphous tumors (CAT) of the heart are extremely rare cardiac masses with only forty-two cases reported. They are often asymptomatic but can cause significant sequelae if they embolize or obstruct cardiac flow. This patient was fortunate to have a carcinoid tumor discovered on screening colonoscopy since it led to the discovery of the potentially dangerous cardiac mass. Cardiac CAT was first described by Reynolds et al. in 1997. Cardiac CAT are non-neoplastic, can occur in all four chambers of the heart, are mobile, and have been shown to recur. Histologically, they are characterized by nodular calcium in an amorphous background of degenerating blood elements, fibrous material, and chronic inflammation. The pathogenesis is unknown but have been described in patients with end-stage renal disease and valvular disease. The treatment of choice is surgical removal with consistent follow-up to monitor recurrence. Cardiac CAT can be difficult to distinguish from cardiac myxomas on imaging, but they have distinct characteristics and should be in the differential when working up a cardiac mass.

A CURIOUS CASE OF CANCER

Jeremy Ragsdell, Tobias Vancil

When evaluating a new patient one must always remain objective in their assessment. Throwing aside judgments and using an open and empathetic approach to diagnosing patients can prevent missing the forest while auscultating the trees. In June of 2015 a 33 year old man presented to an emergency department with complaints of subjective fevers up to 40°C, weight loss, and diarrhea. A careful history of this man revealed a prior record of opiate and IV drug abuse, incarceration for one year's duration, and a history of military service. Physical exam revealed a thin, heavily tattooed man with a jaundiced appearance and significant hepatomegaly without tenderness. The patient went on to disclose that he has had severe itching for one year as well as fevers, chills, shortness of breath and night sweats for 6 months.

A workup was begun for HIV, tuberculosis, and Hepatitis. A CBC and BMP of this patient revealed hypokalemia, a white blood cell count of 19,000 cells/mcL with predominant neutrophils, hemoglobin of 8.8g/dL, and platelets of 527. In addition to these findings the patient had elevated liver enzymes and an albumin of 2.3g/dL. The hepatitis panel came back negative, as well as the HIV and tuberculosis screens. A chest CT was ordered which revealed significant abdominal lymph node hyperplasia. The patient was scheduled for a lymph node biopsy. During this time the patient continued to show elevated liver enzymes and increasing fatigue, night sweats, and shortness of breath in addition to intractable itching and pain. Evaluation of the lymph node revealed significant eosinophilia and diffuse sclerosis with staining positive for CD15 and CD30. A diagnosis of Hodgkin's Lymphoma, nodular sclerosing variant, was made and the patient was scheduled for staging via bone marrow biopsy.

This case is an example of how a patient can present who tugs at a physician's knowledge of common stereotypes but ultimately leads to a completely unrelated diagnosis. Even a skilled diagnostician can be led astray by preconceived notions about a patient during an initial evaluation and thus must always use an objective and knowledge driven approach to testing and treatment.

THROMBOTIC MICROANGIOPATHY IN SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

Subir Bhatia, Goutham Ganesan, Alex Raufi, Derek Lee, Andrew Nguyen, Shane Knipping, Omar Darwish

CASE PRESENTATION: A 25 year-old Vietnamese female with no significant medical history presents with four weeks of temporal headaches, intermittent nausea/vomiting, facial swelling, urinary frequency, and arthralgias. On presentation, she was tachycardic (118 beats/min) and had mildly elevated blood pressure (132/97), with a physical exam notable for facial swelling, epigastric tenderness, and distal joint tenderness. Initial labs showed massive proteinuria (6.2g/d), hematuria, and elevated serum creatinine (Cr, 1.3 mg/dL). Serology included positive ANA 1:320 with speckled pattern, elevated anti-dsDNA, positive anti-smith Ab, decreased serum C3/C4, and weakly positive direct antiglobulin test. She also had anemia (Hgb 8.7 g/dL) and thrombocytopenia (50,000 platelets/mcL), with elevated LDH (368 U/L) and the peripheral blood smear had marked schistocytosis. Altogether, these findings were diagnostic for systemic lupus erythematosus (SLE) and concerning for microangiopathic hemolytic anemia (MAHA). Renal biopsy showed diffuse proliferative glomerulonephritis without crescents as well as evidence of thrombotic microangiopathy (TMA). Initially, she was started on oral prednisone 60 mg/day, however, given a lack of response, a three-day pulse of IV Methylprednisolone (1 g/day) was attempted. Simultaneously, hydrochloroquine and mycophenolate mofetil (MMF) were added as adjunct therapies. Despite this aggressive regimen, the patient's serum Cr continued to increase and her hemolytic anemia worsened. Hydrochloroquine and MMF were withdrawn due to concern for possible contribution to TMA. She required multiple transfusions of both erythrocytes and platelets, and was additionally treated with cyclophosphamide and rituximab, without significant improvement. Again, given lack of response, plasmapheresis was attempted. Genetic testing for known mutations implicated in atypical HUS (aHUS) susceptibility was performed, but returned negative. After 9 sessions of plasmapheresis, the patient's MAHA improved with lower daily decrements in Hgb, and her serum Cr declined from 2.5 mg/dL to 1.5 mg/dL. At the time of submission, maintenance treatment with eculizumab was being considered.

DISCUSSION: This case demonstrates a diagnostic dilemma involving a patient who presented with newly diagnosed SLE and concomitant hemolytic uremic syndrome (HUS), either secondary to SLE or an atypical variant of HUS. A small fraction of SLE cases (fewer than one percent) are complicated by TMA, a histopathological finding linked to the presence of MAHA and an essential feature of syndromes such as TTP and HUS. Currently there are no specific guidelines on the treatment of HUS secondary to SLE. The mainstay of treatment published case reports of TMA in SLE is plasmapheresis because of its effectiveness in replacing ADAMTS-13 activity in TTP, but the therapeutic rationale in HUS is not well established. The recently developed anti-C5 Ab, eculizumab, provides clinicians with a new therapeutic tool to combat aHUS which, as in the case described above, may represent the only viable option in cases refractory to plasmapheresis.

UPPER GI BLEED SECONDARY TO ESOPHAGEAL VARICES IN THE ABSENCE OF LIVER CIRRHOSIS

Anjali Dixit, MPH Stacy Porter, MD Jason Hom, MD

Objectives: 1) Describe a case of esophageal variceal bleeding in the absence of liver pathology; 2) Review the differential diagnosis and work-up of noncirrhotic portal hypertension; 3) Discuss management of portal hypertension secondary to splenomegaly.

Case: A 23-year-old man with a history of chronic idiopathic thrombocytopenia and B-cell acute lymphoblastic leukemia (B-ALL), in remission for four years, presented to his primary care clinic with five days of hematemesis and melena. He was afebrile and normotensive with a pulse rate of 114. His hemoglobin level was found to be 6.6 g/dl compared to his baseline of 14.5 g/dl. His white cell count was normal and platelet count was stable at 96,000/ μ L. Peripheral blood smear was negative for blasts.

He was hospitalized for blood transfusion and evaluation of presumed GI bleed. Physical exam found no stigmata of chronic liver disease; liver and spleen were non-palpable given significant abdominal musculature. Rectal exam revealed black, guaiac-positive stool. He received two units of packed red blood cells and intravenous fluids. Upper GI endoscopy found multiple >5 mm varices in the lower third of the esophagus, one varix with nipple sign, and portal hypertensive gastropathy. Four bands were placed. Liver function tests were normal, and infectious and autoimmune serologies returned negative. Abdominal ultrasounds with Doppler imaging and elastography found no hepatic fibrosis, hepatomegaly, focal hepatic lesions, or perihepatic thromboses. Ultrasound and CT of the abdomen revealed marked splenomegaly (17.1 cm) along with perisplenic and paraesophageal varices and mild ascites. His portal hypertension was therefore attributed to splenomegaly, likely secondary to B-ALL.

Following esophageal banding, he received optimal prophylactic pharmacologic therapy and his hemoglobin level remained stable.

Discussion: Portal hypertension seldom exists outside the context of liver cirrhosis, particularly in Western countries. Rare cases of noncirrhotic portal hypertension may be categorized as intrahepatic (pre-sinusoidal, sinusoidal, or post-sinusoidal) or extrahepatic (e.g., restrictive cardiomyopathy, splanchnic arteriovenous fistulas). Work-up must include identifying clinical signs of portal hypertension, evaluating patency of perihepatic vessels with imaging and/or liver biopsy, and excluding cirrhosis and other causes of chronic liver disease such as viral or autoimmune hepatitis, alcoholic or nonalcoholic steatohepatitis, hemochromatosis, Wilson disease, primary biliary cirrhosis, and other pathologies such as schistosomiasis.

In this case, the patient's portal hypertension was likely extrahepatic in origin. His splenomegaly, which persisted despite remission of his B-ALL, led to increased blood flow through the splenic vein and resulted in portal vein congestion. His chronic thrombocytopenia may not be idiopathic but rather due to hypersplenism. Cases like this are often associated with hematologic malignancy, and some reports have demonstrated complete reversal of portal hypertension following splenectomy. Outside of surgical intervention, treatment of this condition is limited to endoscopic sclerotherapy, ligation, and pharmacologic management of varices.

A RARE CASE OF HIV-ASSOCIATED MULTICENTRIC CASTLEMAN'S DISEASE

Leila Haghighat, MPhil, Wesley Kidder, MD, Donald Abrams, MD, and Terence Friedlander, MD

Castleman's disease is a group of rare lymphoproliferative disorders that share certain clinical and pathological features, first described in 1954. Two clinical schemes, including one from the National Cancer Institute, have been proposed to define an acute exacerbation of HIV-associated multicentric Castleman's disease (MCD). However, no gold standard exists, and diagnosis is one of exclusion, confirmed by pathology.

A 50-year-old male with a history of well-controlled HIV presented to San Francisco General Hospital with 3 months of worsening non-productive cough, dyspnea, and fatigue. His symptoms started with what he thought was a "bad cold" that did not improve after azithromycin and prednisone, prescribed for community-acquired pneumonia. He also endorsed intermittent fevers, chills, night sweats, loss of appetite, and weight loss.

He presented febrile, hypotensive, and pancytopenic, requiring fluid resuscitation and multiple blood transfusions. LDH was normal, and his CD4+ count was 429 with undetectable viral load. Physical exam demonstrated splenomegaly and mildly tender lymphadenopathy throughout his neck, axilla, and groin. CT imaging confirmed these findings, along with bibasilar septal thickening and scattered pulmonary nodules. Bone marrow biopsy and FNA of cervical lymph nodes were negative for lymphoma. Infectious work-up also returned negative, resulting in discontinuation of antibiotics after a total of 4 days. Because of clinical concern for MCD, excisional biopsy of 2 axillary lymph nodes was performed, and the slides were sent to UCSF Medical Center for additional staining.

Indeed, the tissue was consistent with a diagnosis of a mixed hyaline and plasma variant of MCD, based on pathological changes that included HHV8+ plasmablasts in mantle zones, proliferation of CD138+ plasma cells in the interfollicular area, and hyperplastic CD21+ follicles with double germinal centers.

The patient was given an infusion of rituximab 375 mg/m² and liposomal doxorubicin 20 mg/m². He was discharged stably after 13 days of hospitalization with the plan to repeat treatment every 3 weeks for a total of 4 cycles.

Among HIV+ patients presenting with diffuse lymphadenopathy and B-symptoms, the differential should include MCD. Awareness about MCD is crucial, as accurate diagnosis and treatment result in good prognosis, with 3-year overall survival rates of 81%.

A CHALLENGING AND UNUSUALLY SEVERE PRESENTATION OF SEROSAL-TYPE EOSINOPHILIC GASTROENTERITIS: CASE REPORT

First Author: Ariana A Hosseini, B.S. Other Authors: Nima K Harandi, B.A. & Hershan Johl, M.D.

Eosinophilic Gastroenteritis (EGE) is a rare, poorly-defined disorder characterized by diffuse inflammation of the GI tract and peripheral eosinophilia. Due to its infrequent and often non-specific presentation, patients can endure severe, recurrent episodes without timely and appropriate diagnosis and management. In this case, we report on a particularly unusual presentation of this disease, with several complicating factors, further challenging it's management.

A 40-year-old man with a history of EGE and pustular psoriasis presented with abdominal pain, nausea, vomiting and non-bloody diarrhea for three days after consuming various Filipino foods. He had 10+ episodes of non-bloody, bilious vomiting and diarrhea daily. His abdominal pain was diffuse, yet worse in the right lower quadrant, and aggravated by food intake. Patient was taken for CT Abdomen with contrast and subsequently began to report severe burning and multiple pruritic lesions.

Vitals were stable. Patient was in considerable distress. Exam was significant for abdominal distension with grade 3 ascites, moderate diffuse tenderness to palpation, with severe rebound tenderness in the right lower quadrant. Patient's skin had multiple lesions with signs of excoriation and pustule rupture.

Labs revealed a peripheral eosinophil level of 56.7% (ref. range: <6%), absolute eosinophil level of 11,700 (ref. range: 3-350), and IgE of 2553 (ref. range: <25). CT showed moderate ascites, marked gastric antral and duodenal thickening, consistent with EGE. Despite presenting with an acute, severe flare of known EGE and psoriatic lesions in response to contrast, corticosteroids were held due to patient's noted history of pustular psoriasis flares in response to steroid therapy. Therapeutic paracentesis was performed showing significant ascitic fluid eosinophilia of 84%. Biopsy from EGD exhibited eosinophilic inflammatory infiltrate of the esophagus and duodenum. As a regular diet was advanced the patient's symptoms became more severe.

Ultimately, due to lack of clinical improvement, a short course of IV corticosteroids was started. Eosinophilia decreased as the patient's clinical status improved. On follow-up, patient was able to avoid further treatment with corticosteroids when diligently following a "six-food elimination" diet, removing milk, eggs, soy, wheat, tree nuts, and fish from his diet.

This case highlights a very severe case of serosal EGE, complicated by pustular psoriasis, with remarkably prominent peripheral eosinophilia reaching levels infrequently reported in the literature, and the presence of eosinophilic ascites, a sign of serosal infiltration, and thus the most rare subtype. This case also explores the benefits of typical management with corticosteroids, as well as an alternative dietary approach to controlling EGE and preventing subsequent flares.

MATTERS OF THE HEART: AORTIC VALVE MASS IN A PATIENT WITH CARDIAC AMYLOIDOSIS

Abraar Karan, Devin Lowenstein, Pei-Fen Lin

Introduction: AL amyloidosis afflicts roughly 10% of patients with multiple myeloma and about 2000 Americans per year overall. Of those, roughly 50% have cardiac involvement with a median survival of 6 months if heart failure is present. While intracardiac thrombus predominantly affecting the atrial appendages has been associated with cardiac amyloidosis, there is no mention in the literature of intracardiac mass involving the aortic valve.

Case Description: A 49 year-old female with a history of infantile rheumatoid arthritis, smoking, and recent cryptogenic stroke presented for scheduled removal of a 3 mm mobile aortic valve mass that was incidentally found on transesophageal echocardiogram (TEE) during stroke workup 8 months prior. Of note, the TEE also showed evidence of hypertrophic cardiomyopathy and left ventricular diastolic dysfunction with restrictive physiology and preserved systolic function. Surprisingly, pre-op TEE in the OR showed no evidence of the previously identified mass. The patient developed worsening cough and orthopnea and she was transferred to medicine for treatment of pneumonia and severe sepsis.

Thereafter, she was noted to have a discordantly low albumin (3.4) and high total protein (7.8) – a total protein albumin gap of 4.4 – and workup was started for hyperglobulinemia. She also developed increasing urinary urgency and frequency with urinalysis leading to diagnosis of nephrotic range proteinuria. Initial evaluation was remarkable for elevated IgG (2540) with monoclonal IgG lambda on immunofixation. Subsequent bone marrow biopsy showed lambda restricted plasma cells occupying 60% of the marrow; FISH results showed +1q and t(11;14) with CCND1 loss variant multiple myeloma. Given her restrictive and hypertrophic cardiomyopathy, left bundle branch block, and runs of non-sustained ventricular tachycardia, endomyocardial biopsy was pursued to assess for cardiac involvement. Results showed cardiac amyloidosis with light chain deposits in the vessels and interstitium and positive Congo red staining. An implantable cardioverter defibrillator (ICD) was placed and she was started on lenalidomide, bortezomib, and dexamethasone (RVD) regimen for treatment as well as listed for heart transplantation.

Discussion: Cardiac amyloidosis, although rare, is not an uncommon complication of multiple myeloma, and early diagnosis and treatment are paramount given the rapid deterioration associated with the disease. Cardiac involvement should be suspected in any adult with unexplained heart failure and an echocardiogram showing increased wall thickness with a nondilated left ventricular cavity, particularly when associated with low voltage on electrocardiography, ectopic beats or arrhythmia, and/or conduction block.

The significance, etiology, and fate of the valvular mass in our patient remain unclear. The prevailing theory is that the mass was either an atypical thrombus or a condensed collection of light chain fibrils that either dissolved or embolized peripherally. Almost 30% of patients with cardiac amyloidosis may develop intracardiac thrombi and prophylactic anticoagulation should be carefully considered in high-risk patients.

LITTORAL CELL ANGIOMA OF THE SPLEEN: A CASE REPORT

Maisara Rahman M.D., Trina Mansour M.D.(c), Uns Alwahab M.D.

Introduction: littoral- cell angioma (lca) is a primary benign vascular tumor of the spleen that arises from normal cells lining the sinus channels of the splenic red pulp¹. In the past, cases were associated with visceral epithelial malignancies (colorectal adenocarcinoma in two cases, renal and pancreatic adenocarcinoma in each case) and one case was also associated with an intracranial tentorial meningioma². There have been many scattered reports of lca where patients present with several signs and symptoms to being completely asymptomatic. Although lca has been described as being benign, there are reports that associated lca with visceral malignancies². More importantly, there is a very important association between lca and malignancy. There are 36 reported cases of lca published with 11 of them associated with visceral malignancies and 2 with lymphomas³. Malignancies that may occur include colorectal adenocarcinoma, lung, renal, thyroid, ovarian, testicular and pancreatic carcinomas^{3,4}. There have not been any conclusions to explain why this association exists however, immune system dysregulation may play a role. lca of the spleen may occur at any age with no specific sex preference¹. Patients may present symptomatic with complaints of splenomegaly, abdominal pain, pyrexia of the unknown origin or hypersplenism or patients may be asymptomatic with tumors found incidentally, similar to our case¹. Differentials should include multiple hemangiomas, lymphoma, metastatic disease, disseminated infections caused by fungi, mycobacteria, p. Carinii and sarcoidosis¹. However, most common possibilities include neoplastic or infective etiologies³. Given this association with malignancy, a splenectomy would be considered therapeutic and diagnostic for symptomatic patients. Splenectomy is gold standard of treatment for vascular splenic tumors⁴.

CASE PRESENTATION: We present a case of a 53 year old Jordanian female with an incidental finding of LCA that was discovered during a work up for Pulmonary embolism. Patient's past medical history includes hypertension, asthma, diabetes mellitus type II, chronic dyspnea, and pre-syncope. Multiple Splenic Masses and less than 1 cm pulmonary nodules were seen incidentally on CTPA. Patient then had an extensive workup which included a CT and MRI of Abdomen/Pelvis. CTPA was negative for PE but incidentally found multiple pulmonary nodules up to 4mm in size. CT Abdomen found multiple splenic nodules up to 4 cm in size. Cardiac workup was negative for heart disease. Rheumatologic workup and infectious workup was also negative. A Splenic biopsy was consistent with Littoral Cell Angioma. Malignancy workup was negative except for a multinodular thyroid gland with the largest nodule measuring 1.5 cm in the right lobe. Fine needle aspiration of right thyroid nodule showed focally hypercellular smears with variably-sized small follicles, narrow trabeculae and sheets of cytologically bland follicular epithelial cells including pigmented and Hurthle metaplastic cells suggestive thyroid cancer.

CONCLUSION: Littoral Cell Angioma is a rare primary vascular tumor of the spleen is usually discovered incidentally. Close follow-up and careful investigation for secondary neoplasms with patients diagnosed with Littoral Cell Angioma is recommended given that LCA co-exists with various visceral cancers and lymphoma.

SEPSIS IMPOSTERS IN THE MEDICATED PSYCHIATRIC PATIENT

First Author: Santo Ricceri Second Author: Jacob Izenberg Last Author: Pallabi Sanyal-Dey

Rare complications associated with antipsychotic use, neuroleptic malignant syndrome (NMS) and clozapine-induced myocarditis (CIM) can present with similar clinical findings. Typical cases of NMS are characterized clinically by fever, muscular rigidity, altered mental status (AMS), and autonomic dysregulation; however, atypical cases may present with the absence any one of these. While CIM has been less well characterized clinically, common features include EKG changes, fever, tachycardia, dyspnea, and chest pain. Both conditions typically involve elevated creatine kinase and leukocytosis, but there are no specific biomarkers for either condition, making definitive diagnosis difficult.

A 45 year old, homeless man with poly-substance use disorder, schizoaffective disorder, and hypertension, was brought in by police for assaultive and hypersexual behavior and admitted to the psychiatry service, where he was started on clozapine and given an accidental second injection of haloperidol decanoate soon after his first. Two weeks later, the patient developed fever (39.4), leukocytosis (18.7), tachycardia (109), and worsening AMS; a chest X-ray revealed left lower lobe opacity, and the patient was transferred to the medicine service for sepsis secondary to pneumonia. Clozapine was discontinued and broad-spectrum antibiotic treatment was initiated. Nonetheless the patient remained hypotensive with persistently negative blood cultures. Lower extremity DVT ultrasound was negative, and the creatine kinase peak was 94.

The patient was subsequently transferred to the ICU, where he was tachycardic (140 beats-per-minute) and tachypneic (44 breaths-per-minute). Chest CT angiogram, right upper quadrant ultrasound, urine cultures, and a lumbar puncture (rule out HSV encephalitis) were all negative. However, ST segment changes on EKG accompanied by a troponin leak (peak 3.02) were identified, leading to a cardiology work-up with transthoracic echocardiogram showing inferoseptal wall hypokinesis thought to be CIM. In the ICU his creatine kinase peaked at over 3,000, leading to the diagnosis of NMS, likely secondary to long acting haloperidol decanoate, leading to a prolonged disease course. Dantrolene and bromocriptine were not given due to the lack of muscular rigidity, the primary target for these agents. Finally, after two weeks of supportive treatment, the patient stabilized and returned to the psychiatry service. Differentiating between NMS and CIM proved to be an impossible challenge, in this case. Fortunately, the primary treatment for both conditions is prompt withdrawal of the offending agent and supportive therapy.

This case highlights the diagnostic challenge provided by atypical NMS and CIM in the psychiatric patient. In this case there was a delay in the creatine kinase elevation that mired the clinical picture, illustrating the need for an increased clinical suspicion of NMS or CIM in patients on antipsychotics presenting with fever and leukocytosis. Additionally, differentiating between these two conditions has important psychiatric treatment implications, especially in patients who have only responded to clozapine in the past.

PRIMARY HYPERALDOSTERONISM AS AN UNCOMMON CAUSE OF RHABDOMYOLYSIS

Tiffany Seto, Iqbal Munir MD

A 34 year old female with resistant hypertension, hypokalemia and primary hyperaldosteronism was admitted for acute metabolic encephalopathy, rhabdomyolysis and proximal myopathy secondary to severe hypokalemia. Patient's past medical history included severe hypokalemia requiring multiple hospitalizations and hypertension for greater than 10 years.

Prior to presentation, the patient had been on antihypertensive medications, spironolactone and potassium supplements, but had run out of spironolactone and potassium supplements for the previous four days. The patient had begun experiencing fatigue, weakness, and progressive somnolence before being brought into the ER with an altered level of consciousness. Aside from hypertension, the patient's vital signs were stable upon presentation. EKG demonstrated non-specific ST-T changes. Physical exam was significant for proximal muscle weakness. Lab findings demonstrated profound hypokalemia 1.5 mEq/L and elevated total creatine phosphokinase 6897 U/L. Plasma renin activity was 0.36 ng/ml/hr and plasma aldosterone 15 ng/mL (ARR 514). AM cortisol 19.7 ug/dL. Previous labs include 24-hour serum total catecholamine, dopamine, epinephrine and norepinephrine all within normal limits. CT and MRI of the abdomen revealed a 2.7 cm mass that was suggestive of a lipid rich adenoma.

The patient was treated and subsequently underwent an elective laparoscopic left adrenalectomy. Post-surgically, serum potassium was 3.5 mEq/L and ARR dropped to 7.14. Final pathology revealed a 3.0 cm adrenal cortical adenoma. The patient was discharged with scheduled follow-up at the endocrinology clinic.

DISCUSSION: Rhabdomyolysis is the necrosis of striated muscle leading to release of myocyte contents and intracellular potassium into the bloodstream, leading to hyperkalemia. In patients with primary hyperaldosteronism (PA), mineralocorticoid excess leads to hypokalemia, which can be severe enough to cause rhabdomyolysis. Because rhabdomyolysis is usually associated with trauma, crush injuries, overexertion of muscle and renal disease, rhabdomyolysis caused by hypokalemia secondary to PA is usually missed. To date, only 16 cases of rhabdomyolysis as the first manifestation of PA has been reported in literature.

Primary hyperaldosteronism is a common cause of secondary hypertension. Before surgical resection of a hypersecreting adrenal adenoma, confirmation of the diagnosis and laterality of the adrenal lesion should be done by adrenal venous sampling (AVS); however, this procedure was not performed for our patient due to younger age of onset of the disease and CT/MRI imaging indicating the possible culprit lesion. For patients of advanced age, AVS would be necessary to localize the source of excess aldosterone since non-functioning adrenal incidentalomas are more prevalent in this population and current imaging modalities can only detect adrenal masses >5 mm. It is important to bear in mind that patients with PA are at risk of developing rhabdomyolysis secondary to hypokalemia and AVS is not warranted for all patients.

NECROTIZING MYOPATHY: A RARE BUT DEVASTATING REACTION TO STATINS

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A 77-year-old woman with a history of cerebrovascular accident, non-ischemic cardiomyopathy (EF 30-35%), and hypothyroidism presented with 3 days of progressive ascending weakness and dysphagia. On admission, vital signs were significant for hypotension and tachycardia. Neurologic examination revealed proximal lower and upper extremity weakness. Urinalysis showed large blood, but minimal red blood cells. Laboratory studies were notable for TSH>20 mIU/L, AST of 657 IU/L, ALT of 289 IU/L, and a creatine kinase (CK) of 10,979 IU/L. A thorough history revealed that she had been filling two prescriptions for atorvastatin and taking both 40 and 80 mg tablets daily. Initial differential diagnosis included statin-associated myopathy, hypothyroid myopathy, and Guillain-Barre Syndrome.

The patient was admitted for treatment of rhabdomyolysis. Despite discontinuation of the statin, her CK and creatinine continued to rise. Intravenous fluid resuscitation was initiated, but management of the patient's renal failure was limited by the severity of her cardiomyopathy. On hospital day 3, she was found unresponsive and a code blue was called. She was not resuscitated in accordance with her DNR/DNI wishes and she expired. Cause of death was thought to be renal failure secondary to statin associated immune-mediated necrotizing myopathy. Statin associated immune-mediated necrotizing myopathy is a rare but life-threatening autoimmune disorder characterized by proximal weakness, profoundly elevated CK levels, and in some cases, dysphagia. It may develop years after initiation of statins and often persists despite discontinuation of the offending agent. The disorder is associated with antibodies to 3-hydroxy-3-methylglutaryl-coenzyme A reductase and is diagnosed with a muscle biopsy revealing necrosis in the absence of inflammatory cells. Treatment involves discontinuation of the statin and early initiation of immunosuppression.

Our case illustrates the negative effect of delayed recognition on outcomes. It is important to treat concurrent hypothyroidism, as this may increase the risk for statin myopathy.

This case also demonstrates the importance of conducting thorough medication reconciliations. Upon discharge from a previous hospitalization, our patient was prescribed an increased dose of atorvastatin. She misunderstood that this was intended to replace her prior dose and continued to fill both prescriptions. This type of error, known as therapeutic duplication, occurs in 8% of discharges. Hospital discharge is well recognized as a time during which patients are vulnerable to errors. Up to 70% of patients have a medication discrepancy at discharge and 20% have an adverse drug effect during the following weeks. Similarly, two-thirds of hospitalized patients are affected by errors in medication histories, many made at admission. These errors can be prevented or caught early by taking complete medication histories, clarifying discrepancies between existing lists and patient report, and reassessing the need for each medication during transitions of care.

TREATMENT REFRACTORY HYPERGLYCEMIA IN A MIDDLE-AGED DIABETIC WITH UNRECOGNIZED GLUCOKINASE-MATURE-ONSET DIABETES OF THE YOUNG: WHEN LESS IS MORE IN THE NOT-SO-YOUNG

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Introduction: Mature-onset diabetes of the young (MODY) is a monogenic form of diabetes with numerous subtypes. Glucokinase (GCK)-MODY results from GCK mutations that cause mild asymptomatic hyperglycemia resistant to oral hypoglycemics. Individuals are often misdiagnosed with other forms of diabetes. GCK-MODY portends a low life-time risk for complications; therefore, treatment is not indicated. Identifying at-risk patients and pursuing appropriate genetic testing is essential.

Case: A 58-year-old male with type 2 diabetes since age 43, and without known family history of diabetes, presented for routine care. He has a body mass index (BMI) of 28, but is otherwise healthy and does not have microvascular disease. His fasting glucose readings range from 99-156mg/dL and hemoglobin A1C (HgbA1C) levels remain 7-7.4% despite compliance with high-dose metformin and glipizide. Repeat family medical history revealed recent diabetes diagnoses in his 32-year-old daughter and 12-year-old grandchild. Subsequent genetic testing in the family identified a GCK mutation. He was titrated off medication and continues to maintain HgbA1C levels <7.5%.

Discussion: GCK-MODY, also known as MODY2, accounts for 10-32% of MODY cases and exhibits autosomal dominant transmission. Inactivating mutations in GCK cause aberrant glucose sensing in pancreatic beta cells that induces an increased threshold for insulin secretion while maintaining insulin function and sensitivity. Clinically, individuals display mild asymptomatic hyperglycemia (fasting glucose 97-150mg/dL, HgbA1C 5.8%-7.6%). Since oral agents do not alter the underlying pathophysiology, and numerous studies demonstrate low micro and macrovascular complication rates, treatment is not necessary. GCK-MODY should be considered in young (age<35), non-obese patients with a family history of diabetes in >2 generations. Patients are often misclassified as type 1 or 2 diabetes, gestational diabetes or impaired fasting glucose. GCK-MODY can usually be differentiated from type 1 diabetes through autoantibody testing. As in this case, the presence of asymptomatic hyperglycemia may not be identified at a particularly young age and other diabetes risk factors, such as increased weight, may be present. Furthermore, hyperglycemia may not have been recognized in precedent generations. Poor response to oral agents and recognition of hyperglycemia in subsequent generations may suggest a GCK-MODY diagnosis. If suspected, clinical testing is available for several MODY-related genes, including GCK, and should be pursued.

Conclusion: GCK-MODY is characterized by asymptomatic hyperglycemia and may not be recognized until later in life. Affected individuals are often misdiagnosed and receive unnecessary treatment. A careful review of family history and pursuing appropriate genetic testing is necessary for proper disease management.

BUERGER'S IMITATOR: A CASE OF COCAINE INJECTION MIMICKING THROMBOANGIITIS
OBLITERANS

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Introduction: Thromboangiitis obliterans (TAO), formerly Buerger's Disease, is a small to medium vessel vasculitis that can affect the arteries, veins, and nerves of the extremities of young smoker males. We present a case of a patient who met all diagnostic criteria TAO in the setting of wrist cocaine injection.

Case Presentation: A 37 year old male with history of multiple sclerosis, depression, and poly-substance abuse (current tobacco, remote heroin use) presented with a 5-day history of pain, numbness, and ulcerated lesions of the first three digits of left hand with positive Allen's test. He denied current illicit drug use. Diagnostic work up included ESR, CRP, anti-cardiolipin IgG, lupus anticoagulant, complement levels, ANCA IgG, anti-centromere IgG, SCL70 IgG, and serine protease 3 IgG, all of which were negative, Echocardiogram excluded embolic source. Urine toxicology was positive for cocaine metabolites. Arterial angiogram evidence showed multifocal segment occlusion of multiple digital arteries involving all digits of the left hand, sparing the right hand and left foot. Ultimately, the patient admitted to injecting cocaine into the dorsum of his left hand and wrist, but was concerned of receiving substandard care had he admitted it. Heparin drip was discontinued and patient was started on aspirin.

Discussion: TAO usually presents with ischemia of the distal small arteries, frequently involving more than one limb when explored with an arteriogram. Clinical presentation includes claudication of distal extremities; necrotic ulcerations; thrombophlebitis, Raynaud's phenomenon, abnormal sensory findings, and positive Allen's test. Acute phase reactants, immunological markers and auto-antibodies are non-contributory. Despite a strong association with heavy tobacco use, etiology is still unknown. Diagnosis is made angiographically. The treatment is smoking cessation. Multiple diagnostic criteria have been proposed for Bueger's Disease, recently Olin suggested the following diagnostic criteria: (1) onset before 45 years of age, (2) current tobacco use, (3) distal extremity ischemia such as claudication, rest pain, ischemic ulcers or gangrene documented with non-invasive testing, (4) laboratory tests to exclude autoimmune or connective tissue diseases and diabetes mellitus, (5) exclusion of a proximal source of emboli with echocardiography and arteriography, and (6) demonstration of consistent angiographic findings in the involved and clinically noninvolved limbs.

Cocaine injection into the radial artery has also been shown to cause similar symptoms to TAO; however, the symptoms tend to be more severe, have a faster onset and with a clear history of cocaine injection such as our patient. Case reports have shown inadvertent arterial injection of cocaine at the wrist leading to distal vascular compromise. A variety of mechanisms of injury have been proposed including vasospasm, particulate embolization, and endarteritis with resultant thrombosis. Our patient met 5/6 of Olin's criteria. Angiography result suggested an alternative diagnosis; and upon further conversation patient admitted to injecting cocaine in his wrist. This case highlights the importance of complete history taking and its clinical and angiographic correlation in the diagnosis of TAO mimics.

GASTROINTESTINAL INVOLVEMENT AS THE PRIMARY MANIFESTATION OF A CASE OF GRANULOMATOSIS WITH POLYANGIITIS

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Introduction: Granulomatosis with polyangiitis (GPA) is a multisystem disease characterized by immune-mediated destruction of small blood vessels. It commonly manifests with oral, pulmonary, and renal symptoms. Gastrointestinal involvement in GPA is rare, but when implicated can mimic other diseases and make the diagnosis of GPA more challenging.

Case Description: A 34-year-old Hispanic man presented with sore throat, one-month history of bright red, bloody diarrhea, and severe abdominal pain that he had unsuccessfully attempted to control with non-steroidal anti-inflammatory medications. Review of systems was negative for fevers, coughs, shortness of breath, and weight loss. In the preceding year, he developed polyarticular arthritis refractory to prednisone therapy. Physical exam was notable for small ulcerations on his oropharyngeal mucosa and mild bibasilar expiratory-ales on lung auscultation. Notable admission laboratory values included hemoglobin of 6.5 g/dl and erythrocyte sedimentation rate of 118. Rapid strep test, HIV test, blood, stool, and urine cultures were negative. Chest computerized tomography demonstrated bibasilar infiltrates. Colonoscopy and esophagogastroduodenoscopy revealed duodenitis, positive *Helicobacter pylori*, and inconclusive evidence for Crohn's disease. After admission to the medical ward, he was started on intravenous solumedrol. This measure helped control the rectal bleeding but his arthralgia persisted. On hospital day three, the patient developed petechiae on both feet and purpura on his thighs and lower back, which was subsequently biopsied. His urine output became dark and foamy, and urinalysis revealed red blood casts and non-selective proteinuria. Additional laboratory studies were sent at this time, and results were notable for low C4 and positive C-ANCA; IgA levels were within normal limits. Skin biopsy results confirmed necrotizing vasculitis with leukocytoclastic features. A renal biopsy was obtained and revealed pauci-immune, crescentic, necrotizing glomerulonephritis consistent with granulomatosis with polyangiitis. The patient was discharged on combination prednisone and rituximab therapy with subsequent improvement in his rash, arthralgia, and abdominal pain noted at his one-week outpatient follow-up.

Discussion: This case illustrates a unique presentation of GPA with gastrointestinal symptoms as the primary manifestation secondary to splanchnic vessel vasculitis. Our patient's presentation mimicked inflammatory bowel disease and peptic ulcer disease exacerbated by NSAID use. Interpreting these symptoms holistically with the renal and pulmonary findings enabled us to establish the correct, unifying etiology for his presentation. Early recognition of the nuanced and varied presentations of GPA is important as immunosuppression is the therapeutic foundation for the vasculitides, and earlier initiation of therapy can help mitigate associated morbidity and mortality.

DEPRESSION AS SOLE MANIFESTATION OF BRAIN TUMOR

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Learning Objective: To recognize organic brain pathology in patients presenting solely with psychiatric symptoms.

Introduction: Central nervous system tumors are devastating and difficult to detect early on as presenting symptoms may be vague. The prevalence of organic causes leading to psychiatric symptoms, such as anxiety, depression, and psychosis, ranges from 9.1 to 20%. Psychiatric symptoms often improve with psychotropic medications making the diagnosis of the organic source more challenging.

Case Report: A previously healthy 59 year old man presented to his primary care physician with a four month history of depressed mood. His family noticed that he had become more passive, with depressed mood and generalized apathy in the preceding six months. A decrease in job performance required him to go on a leave of absence. Upon presentation, his physical exam was remarkable solely for apathy. Citalopram was initiated without improvement of symptoms. Screening labs for depression were normal. A computerized axial tomography scan (CAT) of the brain revealed a dense mass anterior to the corpus callosum in the frontal lobes bilaterally. Stereotactic brain biopsy demonstrated a type III astrocytic astrocytoma.

Discussion: Butterfly gliomas have bilateral involvement of the frontal or temporal lobes, crossing the corpus callosum. Brain biopsy is the gold standard for confirming the diagnosis as other CNS tumors, such as CNS lymphomas, present with similar radiologic findings. This case is unique in that astrocytic astrocytomas are more frequently found in the pediatric population. The prognosis is very poor with a mean survival of fourteen months in the general population and four to nine months in the elderly. Physicians need to maintain a high index of suspicion when patients presenting with depression fail to respond to appropriate pharmacological therapy. Additional testing is required to exclude organic brain pathology. Due to the rare nature of the tumor, there is a lack of research on astrocytoma tumors in adults.

PAROTID GLAND PRIMARY MANIFESTATION OF MERKEL CELL CARCINOMA

First Author: Bryan Edwards, Tayler van den Akker, Erika Romero Second Author: Damian Casadesus MD.

Merkel cell carcinoma (MCC) is a rare, malignant neuroendocrine carcinoma typically seen in fair-skinned people over the age of 65. It most commonly arises from Merkel cells found in the dermis of the skin, but primary tumors may develop, much less commonly, in extra-dermal sites including the parotid glands. MCCs are most associated with ultraviolet light exposure, impaired immune function, and Merkel cell polyomavirus, an oncovirus found to be integrated in a majority of MCCs.

We describe a case of a 58-year-old Hispanic male, who presented with a primary MCC of the parotid gland, with metastasis to the femur, but no evidence of any primary lesions of the skin. The patient initially presented with knee pain for a 2-week duration, which began spontaneously and without complaints of any constitutional symptoms. A large neck mass was also observed, which the patient stated as painless and growing for the past year. Physical exam showed a non-erythematous knee with pain elicited upon palpation and decreased range in motion. Upon palpation of the parotid mass, it was firm, nontender, and immobile about 2cm in diameter. Exam findings were otherwise unremarkable. Laboratory studies were insignificant with normal calcium and alkaline phosphatase levels. Facial CT revealed two large necrotic masses in the left parotid gland. Fine needle aspiration of these masses confirmed Merkel Cell Carcinoma (MCC). Staging was evaluated with CT imaging of the neck, chest and abdomen revealing necrotic lymph nodes in the submandibular, deep cervical, and anterior cervical regions with possible enlargement of peripancreatic nodes. Additional evaluation for metastasis was warranted due to the knee pain, in which X-ray revealed multiple lytic lesions throughout the distal femur. Confirmatory MRI showed an aggressive intramedullary lesion of the right distal femur with scalloping involving the cortex with extensions into the surrounding structures. These radiographic findings attest to the aggressive nature of MCC. In accordance to the patient, the duration of the MCC parotid lesion growth was less than 1 year, yet resulting in spread to regional lymph nodes, distal femur and knee.

This case joins the few reported cases of primary parotid gland MCC, which serves to physicians and students alike, that this elusive cancer may present anywhere and should be considered when evaluating all masses, however unlikely in location.

LEVEL OF IMMUNOCOMPETENCE AS RISK FACTOR FOR PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

First Author: Lauren M Vaughan

Primary central nervous system lymphoma (PCNSL) is a form of extranodal, high-grade non-Hodgkin B-cell neoplasm. PCNSL originates in the brain, leptomeninges, spinal cord or eyes and rarely spreads outside the nervous system staying limited to the CNS. Although development of PCNSL is often linked to immunocompromised states, most notably patients infected with HIV with low CD4 counts, it is being diagnosed with increasing frequency in immunocompetent patients. While classic immunodeficiency is a clear risk factor, less typical risk factors including autoimmune diseases and iatrogenic immunosuppression warrant further investigation.

A 66-year-old white female presented to the emergency department after a 10-day history of severe nausea and 4-day history of non-bloody, non-bilious vomiting. The previous day she presented to a nearby emergency department with the same symptoms was diagnosed with a likely viral syndrome, given IV fluids and discharged home. She reported associated symptoms of dizziness, lightheadedness, and occasional diffuse pressure-like headaches with photophobia. The dizziness improved while lying down and worsened with movement. She denied fevers, chills, abdominal pain, and chest pain and had not travelled outside of the region. The patient had a past medical history of discoid lupus diagnosed at age 33 and systemic lupus erythematosus diagnosed last year for which she was treated with steroids that were discontinued last month. She was admitted with the working diagnosis of severe dehydration and peripheral vertigo and then prescribed IV hydration, Zofran and Meclizine. The next day the patient reported alleviation of nausea and vomiting. She was tolerating a normal diet and no longer complained of dizziness and was subsequently discharged home. Two days later the patient returned with recurrence of nausea and vomiting with newly developed gait ataxia and occipital head pain described as sharp and stabbing. Her gait was unsteady with dramatic swaying from side to side and inability to ambulate without assistance. CT of the brain was performed demonstrating vasogenic edema within the posterior fossa with mass effect upon the fourth ventricle and suspected early hydrocephalus. MRI showed a well-circumscribed enhancing tumor in the midline of the left cerebellum involving the vermis and extending into the cerebellar hemisphere. She underwent a craniotomy with resection of the tumor with pathology confirming diffuse large B-cell PCNSL. Postoperative staging including eye exam, CT chest, abdomen, and pelvis, PET scan and bone marrow biopsy were negative for lymphoma. Testing for immunodeficiency including hepatitis B and C panel and HIV were negative. The patient did well postoperatively and was scheduled to begin systemic chemotherapy with high-dose methotrexate, Rituxan and Temodar.

This case describes the initial presentation and diagnosis of PCNSL, a condition typically associated with immunodeficiency. Although the patient is seemingly immunocompetent with negative hepatitis panels and HIV, her history of lupus and long-term treatment with steroids could have induced an iatrogenic immunocompromised state predisposing her to the development of PCNSL. This case reinforces the importance of reviewing past medical history and considering non-typical risk factors for the development of disease.

PULSELESS ST-ELEVATION

First Author: Curtis A Hendrix II, MS3 Second Author: Cletus T Moma, MD

Acute ST-segment elevation myocardial infarction (STEMI) requires urgent diagnosis for optimal treatment. However, a small proportion of suspected STEMI's referred for primary percutaneous coronary intervention (PCI) will have a final diagnosis other than STEMI. Knowing the conditions that can mimic a STEMI on an electrocardiogram (ECG), such as acute pericarditis and aortic dissection, is extremely important. These alternative conditions may be as equally life threatening, but require far different treatments.

An 87 year-old female presented to our emergency room with left facial trauma after a fall at her home. She experienced no prodromal symptoms nor loss of consciousness before or after the fall; her only complaint was a painful left wrist. Physical examination demonstrated left peri-orbital swelling and secondary ecchymosis. She was also noted to have an absent left brachial and left radial arterial pulses. The remainder of the exam, including her vital signs, were unremarkable.

Initial diagnostic testing included a 12-lead electrocardiogram which showed diffuse ST-elevation in the inferior and anterolateral leads. Serum troponin was elevated at 1.73ng/mL with a normal serum creatinine. An emergency coronary angiogram was performed, which exhibited mild luminal irregularities in multiple coronary vessels without significant vessel narrowing or occlusion. Subsequent ascending aortic angiography was consistent with an occluded left subclavian artery. A computed tomography (CT) angiogram of the chest demonstrated extensive bilateral pulmonary embolisms (PE) without infarction along with a large thrombus trapped at the origin of the left subclavian artery in the aortic arch. A bilateral lower extremity Doppler ultrasound displayed complete occlusion of the right femoral vein extending to the popliteal vein. A transesophageal echocardiogram visualized a large patent foramen ovale (PFO) along with a large, mobile, pedunculated thrombus (0.68 cm X 2.53 cm) in the aortic arch protruding from the subclavian artery into the descending aorta.

The patient was started on anticoagulation. A repeat CT angiogram three days later demonstrated a decrease in the size of the floating thrombus in the aortic arch. Her symptoms improved with anticoagulation, and she did not require further vascular intervention. The decision was made to manage her PFO conservatively and to continue with indefinite anticoagulation.

This case illustrates the potential for a large bilateral PE mimicking an acute STEMI along with the potential complications of paradoxical embolisms through the use of a PFO. Although rare, it is important to keep this in the differential in the setting of a negative coronary angiogram. Prompt recognition and treatment of alternate causes for STEMI are necessary to improve outcomes, and making a decision on whether to close the PFO or not also becomes a dilemma in trying to obtain the best outcome for the patient.

BLASTOMYCOSIS: A RARE CAUSE OF HYPERCALCEMIA

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A variety of malignancies and certain endocrine, metabolic, and renal disorders can cause hypercalcemia, but to our knowledge, infection with *Blastomyces dermatitidis* has not been previously shown to cause hypercalcemia in humans. A 45-year-old male presented with abdominal pain and severe constipation. The pt was recently diagnosed with right tibia osteomyelitis due to *B. dermatitidis*, and had just completed 14 days of Amphotericin B treatment at the time of admission. Initial labs showed a corrected calcium of 13.9 mg/dL, and the pt was started on intravenous fluids with normal saline to promote urinary calcium secretion. Several doses of calcitonin were administered, but the hypercalcemia failed to fully resolve. The patient was given one dose of zoledronic acid, which rapidly reduced corrected calcium levels to 8.9 mg/dL. Three weeks after discharge, the pt was further evaluated. While the patient still had detectable urine and serum blastomyces antigen levels, which suggested ongoing blastomycosis infection, the patient's calcium levels remained within normal limits. The cause of the hypercalcemia was investigated over the course of hospitalization. Initial workup showed an appropriately low PTH of 13 ng/mL, and a normal phosphorus level of 3.8 mg/dL. The pt was further evaluated for possible malignancy. Parathyroid hormone-related peptide levels were normal at 0.3 pM. His immunoglobulin free light chain ratio was within normal limits, and a SPEP was negative for a monoclonal peak. Skeletal survey, CT chest, and CT abdomen/pelvis was negative for lytic lesions. Without any evidence of malignancy, vitamin D metabolites were further evaluated. The patient had low levels of total vitamin D (17.5 ng/mL), but normal levels of 1,25-dihydroxyvitamin D (35 pg/mL). There was no evidence of sarcoidosis, and ACE levels were within normal limits (26 U/L). TSH levels were low-normal (0.340 mIU/mL), but free T3 and T4 levels were within normal limits, which ruled out possible thyrotoxicosis. A normal bicarbonate level ruled out possible milk-alkali syndrome. The acute rise in calcium strongly argued against familial hypocalciuric hypercalcemia. Review of the patient's medications was also negative for any drugs that promote hypercalcemia. Thus, the most likely cause of hypercalcemia was ongoing blastomycosis. Several accounts of hypercalcemia in animals have been reported, but to our knowledge hypercalcemia secondary to *B. dermatitidis* has not been previously reported in humans. Contrary to reports in animals that suggest a granulomatous etiology, calcitriol levels were normal in this patient. While the precise mechanism remains unknown, the observation that serum calcium rapidly normalized with bisphosphonate treatment suggests that hypercalcemia was likely secondary to osteoclast-mediated bone resorption resulting from osteomyelitis.

‘SPRUE-CING’ UP THE EVALUATION OF CHRONIC DIARRHEA: LET’S LOOK AT THE MEDICATION LIST

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770,000 people are admitted due to adverse drug events annually, with an annual cost of 5.6 million per hospital, making the patient’s medication list an object of scrutiny. Olmesartan is an angiotensin receptor blocker used as an antihypertensive in 1.9 million patients. We describe a patient with long-standing constipation who was ultimately diagnosed with olmesartan associated sprue-like enteropathy.

Our patient is a 90-year-old female who was evaluated for persistent diarrhea over three hospital admissions. She had a history of chronic constipation and hypothyroidism. On examination, her BMI was 21.5 and she appeared cachexic. Medication review revealed omeprazole, levothyroxine, olmesartan, ferrous sulfate, and Culturelle. Laboratory evaluation revealed a non-anion gap metabolic acidosis, acute kidney injury and anemia. Fecal leucocytes, ova and parasites, stool culture, stool guaiac testing, Clostridium difficile antigen, tissue transglutaminase IgA/G antibodies, rotavirus and norovirus assays were negative. VIP and giardia antibody and 5HIAA were negative. Iron studies indicated anemia of chronic disease. Vitamin B12 levels, lipase, lactic acid, and ESR were normal, with a mildly elevated CRP and low vitamin D level. A CT scan of the abdomen was normal. A biopsy during EGD revealed duodenal epithelium with villous atrophy and active chronic inflammation. Immunoperoxidase stains for CD3 and CD8 demonstrated intraepithelial lymphocytes in the villous tips, indicating a celiac disease-like picture. PAS stain was negative for bacillary microorganisms. A literature search revealed the association of olmesartan with a sprue-like enteropathy and olmesartan was discontinued. The patient was started on loperamide and the diarrhea resolved ten days after drug cessation.

The pathophysiology of olmesartan induced sprue-like enteropathy is only theorized at this point. Olmesartan has a higher affinity for angiotensin receptors (AT1) in the gut, whose blockade leads to the unopposed activation of angiotensin receptors (AT2) in the duodenum and jejunum. AT2 activation induces apoptosis of gut enterocytes, ultimately causing overwhelming apoptosis of enterocytes and eventually villous atrophy. Although a systematic re-challenge with olmesartan and repeat biopsy showing villous regeneration is required to confirm the diagnosis, we refrained from confirmation considering the patient’s frailty. 54 cases have been reported with a mean age of 69. We believe, at 90 years old, our patient is the oldest reported person who suffered from olmesartan-induced sprue-like enteropathy. It is possible that her symptoms were masked by the long duration of constipation.

In conclusion, this case illustrates the importance of reviewing the medication list for possible side effects when developing a differential. Raising awareness of possible side effects is critical in avoiding preventable morbidity, mortality and healthcare costs.

EMPHYSEMATOUS GASTRITIS COMPLICATING ENTEROPATHY-ASSOCIATED T-CELL LYMPHOMA: A RARE COMPLICATION OF A RARE CANCER

Anthony Simone BS, Teresa Lynch MD FACP, Jacqueline Fischer MD FACP

Case: A 23-year old male recently diagnosed with Enteropathy Associated T-Cell Lymphoma (EATL) Type II presented at day 3 following his first cycle of CHOEP (cyclophosphamide, doxorubicin, etoposide, vincristine and prednisone) with neutropenic fever (102.8F, white cell count 100 / uL) nausea, vomiting, and periumbilical pain radiating to the back. Examination revealed a cachectic young man with sinus tachycardia, dry mucous membranes and periumbilical tenderness. Empiric ertapenem, piperacillin-tazobactam and filgrastim were begun and the patient's fever and neutropenia resolved. However, there was progression of periumbilical tenderness and the new development of abdominal distension over the ensuing 4 days. Abdominal computed tomography (CT) scan revealed curvilinear air dissecting the gastric wall. Esophagogastroduodenoscopy (EGD) followed which revealed beefy red gastric mucosa and diffuse nodularity. A clinical diagnosis of emphysematous gastritis was made and the patient was transferred to a higher care facility. The patient was placed on strict NPO status and was managed conservatively with intravenous fluids, pantoprazole, meropenem and vancomycin. The patient stabilized, his abdominal pain resolved and a repeat CT scan 5 days later demonstrated resolution of gastric intramural air. Antibiotics were discontinued, and the patient's diet was advanced as tolerated. During this hospitalization, the patient was deemed stable to begin cycle two of his CHOEP regimen, which he completed without complications. On hospital day 23, the patient was discharged after overcoming the high morbidity and mortality associated with emphysematous gastritis—a rare and highly fatal gastrointestinal disorder.

Discussion: Enteropathy-Associated T-cell Lymphoma (EATL) represents only 5% of all gastrointestinal lymphomas and has an incidence of 1 per million. Emphysematous gastritis is even rarer and often fatal, with fewer than 50 cases reported in the literature since 1889 and mortality rates of 61%-80%. Erosion of the gastric wall due to ingestion of corrosive substances (24% of cases) and alcohol abuse (22% of cases) are the most common predisposing factors. Patients who are immunocompromised are at an increased risk for developing emphysematous gastritis, and 10% of reported cases involve an underlying malignancy. Ours is the first known case of emphysematous gastritis complicating EATL.

Emphysematous gastritis most often presents with features of the systemic inflammatory response syndrome coupled with abdominal pain or gastrointestinal bleed. Intramural air in emphysematous gastritis usually results from mucosal invasion of gas-producing bacteria, and common isolates include *Escherichia coli*, *Enterobacter* species, *Pseudomonas aeruginosa* and *Clostridium perfringens*. Management is supportive with severe cases of infarction or frank gastrointestinal perforation requiring surgical intervention.

UNUSUAL PRESENTATION AND SEQUELAE OF ORBITAL CELLULITIS

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Orbital cellulitis is an infection occurring posterior to the orbital septum and can lead to life-threatening sequelae such as optic neuritis, intracranial abscess, and cavernous sinus thrombosis (CVT). As such, it must be differentiated from preseptal cellulitis, and requires rapid diagnosis with prompt therapy.

A 72-year-old female with history of diabetes presented with left-sided upper jaw pain, chills, eyelid and facial swelling for two weeks. IV ampicillin-sulbactam was begun for preseptal cellulitis until CT brain revealed left periorbital edema with ophthalmic vein enlargement. The antibiotics were changed to IV vancomycin and meropenem for orbital cellulitis and the patient was transferred for further work-up. Upon transfer, she endorsed mild left orbital pain. Physical exam revealed severe bilateral periorbital edema, proptosis, injection, chemosis, and impaired extraocular movements. The next day, the patient developed 20/70 left visual acuity impairment, and had intermittent fevers as high as 38.2C, lasting up to 18 hours and resolving without intervention.

MR venogram revealed leptomeningeal enhancement suggestive of meningitis. Lumbar puncture revealed critical hypoglycorrhagia (16mg/dL), elevated protein (99mg/dL) and pleocytosis (1600 WBC/uL) with neutrophilic predominance (59%) in the cerebrospinal fluid. However, microscopy and culture tested negatively for bacteria, fungi, and tuberculosis. The dose of vancomycin and meropenem doses were increased to better penetrate CNS (1.75g to 2.5g and 500mg to 2g per day, respectively), with resolution of periorbital edema, chemosis, and visual impairment the following day. Despite clinical improvement, repeat LP revealed persistently abnormal results (23mg/dL glucose, 98mg/dL protein, 925 WBC/uL, 52% neutrophils), with continued negative CSF microscopy and culture. Therefore, brain MRI was ordered, which showed left orbital abscess, subdural empyema in the left temporal fossa floor, persistent meningitis in the left sylvian and suprasellar cisterns, and CVT. Consequently, the patient underwent a left-sided craniotomy for evacuation of subdural empyema without complications. Intraoperative culture of drained fluid was negative.

Subdural empyema is an uncommon complication of orbital cellulitis, and its location in the left temporal fossa floor as in this case is exceedingly rare. In addition, this case was highly unusual due to the patient's largely benign clinical presentation despite presence of extensive intracranial infection. Throughout the hospitalization, she denied headaches, nuchal rigidity, nausea, or vomiting. Moreover, neither orbital cellulitis nor CVT usually present with bilateral proptosis, and CSF and intracranial drainage tested negatively despite remarkable hypoglycorrhagia on LP. The profoundly atypical presentation in this case illustrates the need for heightened clinical suspicion for complications in cases of orbital cellulitis. Prompt imaging is required to diagnose intracranial sequelae such as CVT or abscess. Use of MRI to evaluate the recurrent low-grade fever after 48 hours of IV antibiotic therapy helped establish the need for surgical intervention to prevent permanent visual defect or mortality.

SEPTIC SHOCK SECONDARY TO A URINARY TRACT INFECTION WITH *PEDIOCOCCUS PENTOSACEUS*

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Introduction: *Pediococci*, a group of lactic acid bacteria, are facultative anaerobe, catalase-negative, gram-positive cocci. This species is normally found in the flora of the oral cavity and alimentary tract. It can also appear in plants, meat products, and dairy products. Recently, *Pediococci* have caused opportunistic infections in humans, posing a challenge to treatment due to resistance to multiple antibiotics, including glycopeptides. Although vancomycin is typically the drug of choice for many hospital-acquired infections caused by gram-positive bacteria, the increased prevalence of vancomycin-resistant species such as *Pediococcus* has posed a challenge for clinicians.

Case Description: The patient is a 70-year-old male with a past medical history of benign prostatic hyperplasia, type 2 diabetes mellitus, hypertension, depression, and alcohol abuse. He presented to the emergency department from home after his family called paramedics because they had not heard from him in three days. He was found to be hypotensive with a blood pressure of 91/52 mmHg, tachycardic with a heart rate of 123 beats per minute, and tachypneic with a respiratory rate of 24 breaths per minute. Temperature was 98.8 °F. White blood cell count was 13,700 cells/mcL. Creatinine was 7.52 mg/dL (baseline was 0.8 mg/dL four months prior to admission). Urinary catheter was placed, and 2.5 L of urine were drained. Urinalysis revealed 10-25 white blood cells, 2+ bacteria, minimal squamous cells, and trace leukocyte esterase. Physical exam revealed a palpable distended bladder with tenderness to palpation. He was admitted to the intensive care unit due to concern for septic shock. He required intravenous fluids and was started on vasopressors. He was empirically started on broad-spectrum antibiotics, including vancomycin and piperacillin/tazobactam. Urine culture from admission revealed a final result of *Pediococcus pentosaceus* (100 CFU/HPF). Vancomycin was discontinued due to lack of activity against this organism. The patient received a total of 10 days of piperacillin/tazobactam (3.375 grams IV every 8 hours with appropriate dosage adjustment for renal function). Repeat urinalysis and urine culture were done on day 5 and showed resolution. Upon discharge, sepsis was resolved, and creatinine was back to baseline.

Discussion: To the best of our knowledge, this is the first case report that describes the successful use of piperacillin/tazobactam to treat septic shock and acute kidney injury in a patient whose urine culture was positive for the organism *Pediococcus pentosaceus*. With this antibiotic treatment, IV fluid hydration, and vasopressors, our patient improved clinically, and his kidney function returned back to baseline. This case report emphasizes the importance of vancomycin-resistant organisms as pathogens. This serves as an alert to clinicians in medical decision-making of selecting antibiotic coverage for gram-positive cocci of urinary source where resistances and sensitivities may not be available.

WHAT YOU DON'T EAT MAKES YOU BLEED

Dillon Li, Charles Bodine, Sally Nau.

A 43 year old male presented to the emergency department (ED) with left lower extremity (LLE) pain, redness and swelling. The swelling started three weeks ago on top of multiple open lesions on both legs. Patient received steroid treatment for suspected Henoch-Schonlein purpura. However the lesions aggravated despite the treatment leading to current ED visit. In the ED, patient's blood pressure was 98/60 and heart rate was 112. For suspected cellulitis and sepsis, patient was admitted and received antibiotics treatment.

Patient denied recent trauma, long distance travel, and prolonged bed rest. Past medical history was insignificant. Physical exam showed diffused redness and swelling in entire left leg with multiple purpuric ulcerated lesions. Similar lesions were also found on right leg. Patient was a smoker but denied alcohol or illicit drug use. Patient was in a monogamous relationship and had no recent sick contact.

Cellulitis was considered less likely as patient remained afebrile and similar lesions were noticed on both legs. Deep vein thrombosis was ruled out by lower extremity duplex scan. LLE radiography showed soft tissue swelling but no signs of necrotic fasciitis or osteomyelitis. Vasculitis studies were negative for hepatitis panel, HIV1/2, ANA, ANCA, cryoglobulin, rheumatoid factor and showed normal C3, C4 levels. Skin biopsy of the lesions returned as mild dermatitis with hemorrhage and was negative for vasculitis.

Patient was anemic with hemoglobin dropping from 7.8g/dL to 6.6g/dL over 48 hours with worsening LLE redness and swelling. Patient was transfused twice during hospitalization. Complete blood count study revealed normocytic anemia with increased red cell distribution width (RDW). Labs were significant for very low level of folate, low albumin and borderline low level of B12. Iron study and peripheral blood smear supported iron deficiency anemia in the context of folate deficiency. Nutritional deficiency was suspected. Upon further inquiry about dietary pattern, patient admitted never eating fruits and vegetables. Vitamin C level was ordered while mega dose of vitamin C was started. Patient responded to vitamin C replacement quickly. Over 48 hours the hemoglobin increased from 7.5 to 9.9 g/dL and the redness and swelling of LLE diminished rapidly. Vitamin C level later returned as extremely low, confirming the diagnosis of scurvy presenting as lower extremity bleeding.

This case illustrated the importance of including micronutrient deficiency in the differentials of challenging cases. Extremely unbalanced diet without green vegetables and fruits intake can lead to vitamin C deficiency which causes poor collagen synthesis, exhibiting poor dentation and poor wound healing. Vitamin C is also required for optimal iron absorption, therefore vitamin C and folate deficiency can cause a normocytic anemia with wide RDW. Scurvy, a medieval legendary disease among sailors, can still ail who does not eat greens in modern America.

KILLER SEX: CASE OF SUBARACHNOID HEMORRHAGE MASKED AS ST-ELEVATED MYOCARDIAL INFARCTION.

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The differential diagnosis for pulseless electrical activity (PEA) is broad. When encountering PEA, common causes come to mind: hypoxia, pulmonary embolism, metabolic toxicity and electrolyte abnormalities. Subarachnoid hemorrhage (SAH) is a common neurological disorder that leads to an out-of-hospital (OOH) cardiac arrest. Patients who experience a cardiopulmonary arrest out of hospital secondary to SAH can also present with electrocardiogram (ECG) abnormalities that mimic another medical emergency: acute coronary syndrome (ACS). There is limited exploration to why such ECG abnormalities present with SAH. We present a case of a gentleman who presented with an OOH witnessed PEA arrest while having sexual intercourse with a stranger.

A 59-year-old African American male with an unknown medical history was brought to the emergency room via ambulance after being found unresponsive during sexual intercourse. He lost consciousness and his partner called 911 and initiated cardiopulmonary resuscitation (CPR). In route to the hospital, the patient had return of spontaneous circulation (ROSC) with an estimated down time of approximately 10 minutes. Upon arrival to the emergency room, the patient again experienced PEA. In the span of twenty minutes while in the emergency department, the patient experienced three more PEA episodes. Each time, advanced cardiac life support (ACLS) was followed and ROSC was achieved. The presenting ECG on arrival to the hospital demonstrated ST-segment elevations with inferior wall distribution. Subsequent ECG's showed various ST-segment elevations and depressions. Based on the history of his activity leading up to the arrest, a ST-segment elevated myocardial infarction (STEMI) was thought to be the cause of the cardiac arrest. On physical exam, the patient was intubated and had a Glasgow Coma Scale (GCS) of three. Troponin levels were within normal range. Heparinization and targeted temperature management (TTM) were suggested. Before proceeding with either treatment modality, the cardiologist requested computed tomography (CT) without contrast to rule out bleeding. The CT scan revealed extensive subarachnoid hemorrhage with early-generalized cerebral edema. Heparin therapy and TTM plans were aborted given the setting of active intracranial bleeding.

There are limited studies and data as to why ECG changes occur with SAH. Some studies point to "stunned myocardium" and coronary vasospasm as a cause. In some animal studies, neurogenic origin seems to cause the ECG abnormalities by alteration of sympathetic tone to the heart. In our patient, to think sexual activity led to a STEMI and his cardiac arrest was not unreasonable. In broadening our differential as to what caused the PEA arrest, we found the SAH and this stopped our medical team from potentially administering therapies that are contraindicated in the setting of active intracranial bleeding.

ASPERGILLUS FUMIGATUS: A RARE CAUSE OF VERTEBRAL OSTEOMYELITIS IN AN IMMUNOCOMPETENT PATIENT

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Introduction: Vertebral osteomyelitis is a rare cause of back pain and can develop from direct trauma, underlying adjacent infection, or hematogenous spread from distant sites. Untreated vertebral osteomyelitis can lead to significant neurologic deficits and spine deformity. *Staphylococcus aureus* is the most common single pathogen. IDSA guidelines recommend confirming suspected osteomyelitis with MRI and biopsy, then initiating appropriate antimicrobial treatment. Here, we describe a case of vertebral osteomyelitis caused by an atypical pathogen, *Aspergillus fumigatus*.

Case: A 54 year-old-male from Senegal with a medical history of uncontrolled asthma and hypertension was admitted for low back pain present for three months. Four months prior, he had been admitted for respiratory failure from asthma, requiring mechanical ventilation and central venous line placement and was eventually discharged. Since that initial admission, he reports “electric” pain in the lumbar region that radiates down both lower extremities. He denied any trauma, spine injections, surgeries, intravenous drug use, or infections. Physical examination was remarkable for lumbar spine point tenderness. There were no signs of erythema, abrasion, ecchymosis, or inguinal lymphadenopathy. Neurologic exam was normal.

Initial laboratory tests revealed white blood cell count of 11.8 billion/L, elevated erythrocyte sedimentation rate of 43 mm/hr and hemoglobin A1c of 8.6. Lumbar x-ray and MRI revealed suspected osteomyelitis of L2-L3. Human immunodeficiency virus screen was negative. Due to the patient being from Senegal, tuberculosis quantiferon was ordered and positive, although there was no suspicion for active TB. He underwent a contrast-tomography-guided vertebral biopsy, after which he was started on empiric antibiotics. After eight days of incubation, biopsy culture returned positive for *Aspergillus fumigatus*. A serum galactomannan also returned positive. Intravenous voriconazole therapy was added to the empiric antibiotic regimen. He underwent a laminectomy, debridement, and vertebral fusion. No granulomas, malignancy, or bacteria were found and GMS stain of the surgical specimen showed fungal hyphae. He was taken off of empiric antibiotic therapy and continued on oral voriconazole. He clinically improved with resolution of pain and discharged with a twelve-week course of oral voriconazole.

Discussion: After further review of this case, the likely route of the patient’s osteomyelitis appears to be secondary to hematogenous dissemination. The source is likely from past central line during previous intensive care unit hospitalization in the setting of high dose intravenous steroids and uncontrolled type 2 diabetes mellitus. *Aspergillus fumigatus* is a rare cause of vertebral osteomyelitis, especially in immunocompetent individuals. The patient has no knowledge of prior *Aspergillus* infection and showed no other clinical manifestations of Aspergillosis. Only 180 well-described cases of *Aspergillus* osteomyelitis are documented in the English literature from 1947 to 2013. This case highlights the importance of considering nosocomial infection as a cause of back pain, and rare pathogens as a cause of osteomyelitis.

OSTEOGENESIS IMPERFECTA: STICKS AND STONES MAY BREAK MY BONES, BUT SURGERIES WON'T HURT ME

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Introduction: Osteogenesis Imperfecta (OI) is a rare, inherited connective tissue disorder that affects less than 1 in 20,000 individuals. The disease is characterized by brittle bones stemming from mutations that affect the production of alpha chains in type I collagen. This leads to a distinctive phenotype that involves compromised integrity of bones, tendons, ligaments, skin, and sclera. OI patients are typically managed conservatively with pharmacologic and physical therapy rather than surgery due to the risk of intraoperative injury. We present a unique case of OI where the patient's independence and quality of life are improved with multiple orthopedic surgical interventions.

Case Description: A 4-feet tall 41-year-old woman weighing 80lbs presented to the physician with longstanding history of pain, arthritis, and instability in bilateral knees. After a year of conservative management, the patient had diagnostic right knee arthroscopy which revealed dysplastic changes and partial tears in both the ACL and PCL as well as the medial meniscus. During this time, the patient was noted to have significant spinal scoliosis, joint laxity in her brachydactylic digits, and blue-tinged sclera. Combined with her extensive history of bone injuries, a clinical diagnosis of OI was made, and the patient and her physician decided to continue conservative treatment at this time. Less than two years later, the patient began experiencing frequent falls which ultimately led to severe pain in her right knee. Orthopedic surgery intervened to do a total knee arthroplasty with the goal of managing her pain. Although the patient sustained a fracture to her femoral medial condyle intraoperatively, the surgery was successful in enhancing her independence. Over the course of the next five years, the patient suffered significant osteoporotic changes in bilateral hips, likely secondary to compromised bony infrastructure. Decreased mobility and excruciating pain in her hips led the patient to opt a second time for surgery. The total hip arthroplasty relieved her pain to restore independence and quality of life once more despite her disease.

Discussion: There is currently no cure for OI. The goals of therapy are typically conservative, centered on reducing fractures, preventing bony deformities, and minimizing pain with physical therapy and pharmacologic interventions. Surgery is less commonly involved in OI cases due to the increased risk of new fractures. However, our patient was unique in that surgical interventions managed her disease process unusually well. Multiple orthopedic surgeries not only enhanced function of her limbs but also improved her quality of life by reducing pain and restoring her independence. Wide-ranging variability both between and within the types of OI suggests that we should consider more than the standard treatment for each patient using a patient-centered approach to ensure optimal management.

PAZOPANIB INHIBITS VASCULAR ENDOTHELIAL GROWTH FACTOR SYNTHESIS IN HUMAN RETINAL PIGMENT EPITHELIAL CELLS

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Age-related macular degeneration (AMD) and associated proliferative vitreoretinopathy (PVR) affects over 2 million people in the United States, and is a leading cause of blindness in people over 50 in developed nations worldwide.

The human retinal pigment epithelium (hRPE) is a monolayer of epithelial cells between the neural retina and choroid. hRPE cells are normally mitotically inactive after early fetal life. They metabolize and transport nutrients to the neural retina, dispose of waste and protect the photoreceptor cells. AMD is associated with the development of choroidal neovascularization and abnormal vitreoretinal proliferation. Since hRPE cells are a major source of angiogenic factors, like VEGF, they may play a role in the development of these complications, and inhibiting overproduction of VEGF by hRPE may have therapeutic value in prevention or treatment.

Since pazopanib (PZB) is a tyrosine-kinase inhibitor of VEGF R1/VEGF-R2 and has been proven to be an effective treatment for various types of cancer, we investigated if it has any effect on hRPE cell proliferation and VEGF synthesis. We show that PZB inhibits hRPE cell proliferation and inhibits VEGF synthesis in hRPE cells, and therefore it may be of therapeutic value in AMD.

CONVERSION DISORDER PRESENTING AS NEW ONSET PARAPLEGIA IN A PATIENT WITH HUNTINGTON DISEASE

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INTRODUCTION: Conversion disorder is a disease entity that typically develops many years after the inciting event and has a poor prognosis with significant disability. When conversion disorder presents concurrently with other neurological disorders, such as Huntington disease, it poses a diagnostic challenge.

CASE: A 33-year-old Caucasian woman with a past medical history significant for Huntington disease, depression, and anxiety presented with paraplegia consistent with a T10 spinal cord injury (SCI) after an unwitnessed fall down 6 stairs. Physical exam upon presentation was significant for decreased rectal tone, lower extremity hyperreflexia, total anesthesia below the umbilicus, decreased bilateral lower extremity muscle tone, and loss of volitional movement below umbilicus. MRI of head, neck, and spine showed no evidence of traumatic spinal cord compression or vertebral fracture. Following negative repeat imaging, she developed new symptoms including urinary incontinence with stool retention and return of sensation in her right first toe. Physical medicine and rehabilitation examination also revealed neurologic findings inconsistent with her initial exam, including use of abdominal and adductor muscles. Upon further conversation with psychiatry, it became clear that the patient was experiencing significant social stress including sexual and physical abuse from an individual who had recently reentered the patient's life. She additionally exhibited lack of concern, or *La belle indifférence*, for her new paralysis, which is consistent with conversion disorder. Care teams discussed best treatment and determined she would be best served by continued encouragement and supportive, multidisciplinary care in the form of psychological therapy, physical therapy, and occupational therapy. The patient was transferred to acute inpatient rehabilitation, where she experienced functional gains and was discharged to her home where she lived independently with the use of assistive devices.

DISCUSSION: Conversion disorder is characterized by neurological symptoms that are inconsistent with a neurological disease but cause distress and/or impairment. Predisposing factors include personality factors, disease, coping style, childhood abuse, and poor family functioning. Prognosis for conversion disorder is poor. Factors related to a favorable outcome include early diagnosis and intervention, presence of depression and anxiety, positive response to initial treatment, and a therapeutic relationship with healthcare providers. The most effective treatment for conversion disorder has been shown to be education about the diagnosis from a provider with whom the patient has a therapeutic alliance. This case demonstrates an impressive recovery from total paraplegia secondary to conversion disorder following rapid intervention from a multidisciplinary care team. Effective communication between medical teams allowed formulation of a unified care plan that assisted with patient recovery, demonstrating the positive effects of care coordination and communication.

A STUMP THAT STUMPED US

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Introduction: Of rare frequency, carotid stump syndrome is characterized by recurrent transient ischemic attacks ipsilateral to an occluded internal carotid artery. Microemboli from the occluded internal carotid artery stump migrate into middle and anterior cerebral artery circulation through external carotid-internal carotid anastomoses.

Case Description: A 48-year-old male, with history of smoking, hypertension and hyperlipidemia, admitted to our hospital for recurrent ischemic attacks in very brief intervals. He consulted his primary care physician after experiencing a 2-week history of recurrent transient loss of vision in the right eye. Before obtaining the carotid ultrasound to which he was referred, the patient experienced another self-limiting event August 7, 2015. This episode involved numbness and loss of strength in his left extremities with slurred speech. Computed tomography (CT) obtained of the head was negative for acute intracranial processes. Carotid duplex ultrasound showed 100% occlusion of the right internal carotid artery (ICA) and 20-49% occlusion of the left ICA. After resolution of symptoms and medical management with Aspirin, the patient was discharged home on August 8, 2015.

Again the patient experienced left-sided weakness and speech impairment, and was consequently readmitted the next day. Repeat head CT was unremarkable. Diffuse weighted imaging showed multiple infarcts scattered throughout the right frontal, parietal and occipital lobes. Magnetic resonance angiography of the brain and neck showed collateral flow and opacification of the right anterior and middle cerebral artery, as well as complete occlusion of the right ICA. There were no stenotic lesions in the intracerebral or extracerebral arteries. The patient was discharged August 13, 2015 with addition of Plavix for dual antiplatelet effect and recommended to cease smoking.

One week later (August 20, 2015), recurrence of transient right-sided blurring of vision and left-sided hemiplegia and hemiparesthesia readmitted the patient. Repeat head CT was again unremarkable. The clinical picture was deemed consistent with right carotid stump syndrome. CT angiography of the head and neck revealed right ICA occlusion from the cervical bifurcation to the intracranial ICA. It was decided to proceed with stent assisted coil embolization of the right carotid stump on August 25, 2015. After close monitoring and resolution of symptoms, the patient was discharged on Plavix and Aspirin. The patient remained symptom free after 3-month follow up.

Discussion: Although rare, this case reinforces the importance of considering carotid stump syndrome as a cause for recurrent transient ischemic attacks or stroke in patients with unknown etiology, especially when patients with a known ICA occlusion experience repetitive ipsilateral retinal and contralateral body symptoms. Increasing awareness and recognition of this treatable syndrome is a critical step towards decreasing the morbidity associated with undiagnosed cases.

CHRONIC EOSINOPHILIC PNEUMONIA MIMICKING COPD EXACERBATION

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Introduction Chronic eosinophilic pneumonia (CEP) is a rare disorder with incidence estimated at 0.23 cases/100,000 population per year in a recent study.¹ CEP is characterized by marked accumulation of eosinophils in the interstitial and alveolar spaces of the lungs.² Typical symptoms include productive cough, fever, breathlessness, weight loss, and night sweats.³

Case Presentation A 70-year-old white male veteran with chronic obstructive pulmonary disease (COPD) and lung adenocarcinoma successfully treated with right upper lobectomy in 2004 presented with a three-week history of shortness of breath, nonproductive cough, and increasing home oxygen requirement. The patient was chronically on two liters home oxygen therapy but had recently required four liters home oxygen prior to admission. He also reported being a former smoker with 200 pack-year smoking history and noted recurrent episodes of pneumonia since childhood. He was afebrile with stable vitals on initial presentation. Physical examination of lung fields demonstrated expiratory wheezes in the left lower posterior lobe with other lobes clear to auscultation bilaterally. Laboratory studies were notable for elevated white blood cell count at 11.7 K/cmm with 49.8% eosinophils on differential. Absolute eosinophil count was elevated at 4.9 K/cmm. Chest radiography showed evidence of lung scarring and patchy bilateral infiltrates. Computed tomography (CT) of the chest without contrast demonstrated chronic postsurgical changes and interval development of bilateral patchy infiltrates throughout the lungs. He was started on levofloxacin and ipratropium/albuterol for suspected COPD exacerbation and bacterial pneumonia. Pulmonology was consulted and performed bronchoalveolar lavage (BAL) with bronchoscopy. BAL differential results showed 77% eosinophils. Pulmonology believed this to be CEP and recommended treatment with prednisone 40 mg PO daily. Steroid therapy was initiated and the following day he reported symptomatic resolution. At that time, his WBC was within normal limits and differential now showed 2.3% eosinophils. Absolute eosinophil count had also returned to normal limits at 0.2. Blood, urine, and BAL cultures returned no growth. *Streptococcus pneumoniae* and legionella urinary antigens were also negative. He was discharged home to complete a steroid taper. At most recent follow-up, he was asymptomatic and reported resolution of nearly all of his pulmonary complaints.

Discussion This case demonstrates why CEP should be considered in the differential diagnosis of any patient who presents with pulmonary complaints and considerable peripheral eosinophilia. BAL showing = 25% eosinophilia nearly clinches the diagnosis.⁴ Prompt recognition and diagnosis can lead to appropriate therapy, with most patients seeing dramatic resolution of symptoms one or two days after corticosteroid administration.⁴

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CHAPTER WINNING ABSTRACT: THE RESURGENCE OF THE GREAT MASQUERADER: SYPHILIS AWAKENS

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Introduction: Syphilis cases have rebounded after being on the verge of elimination from the United States in the year 2000. Interest in syphilis has been rekindled among clinicians as rates of primary and secondary syphilis increase and the epidemiology changes. We describe a case exhibiting the resurgence of this age-old disease. This patient presented to us with visual complaints related to ocular syphilis as a primary manifestation of underlying and previously unknown HIV.

Case description: 6 weeks after suffering from a diffuse maculo-papular rash originally diagnosed as viral exanthema, a 60-year old heterosexual Caucasian male returned to clinic with weight loss, desquamation of the hands and feet, and partial vision loss of the right eye. Ophthalmology referral resulted in the diagnosis of acute syphilitic posterior placoid chorio-retinitis. Follow-up laboratory studies confirmed the diagnosis of syphilis with a reactive RPR and MHA-TP. CSF VDRL was negative. Subsequent analysis revealed the patient was positive for HIV-1 Antibodies via Western Blot. HIV-1 Viral load was determined to be 8,746 copies/ml. CD4 count was 663 cells/mcl. The patient was treated with 2 weeks of intravenous penicillin and started on HAART with Atripla.

Discussion: The above case highlights the outbreak occurring throughout the United States. Further, this case exemplifies the changing epidemiology of syphilis to affecting others outside of the African American and MSM population. Physician and population awareness of the increasing incidence, symptoms and sequelae of this disease as well as timely screening and diagnosis of individuals with risky behavior patterns should be emphasized. It takes combined efforts from physicians belonging to primary care, ophthalmology and infectious disease to provide timely and effective therapy to ensure quick recovery of these patients.

CYTOMEGALOVIRUS INFECTION AND DIABETES INSIPIDUS: IS THERE A LINK?

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Introduction: Very few cases have been reported of central diabetes insipidus (CDI) secondary to Cytomegalovirus (CMV) encephalitis. We report a case of CDI due to CMV encephalitis in an immune-compromised patient.

Case presentation: A 44 year-old African American female with a past medical history significant for AIDS presented to the emergency room complaining of abdominal pain, worsening diarrhea for the last week, and was noted to have altered mental status. Patient was non-compliant with antiretroviral therapy (ART). Her last CD4 count was 5 cells/mm³ one year prior to this admission. On presentation, vital signs were stable. Patient was alert but not oriented, and was visibly tremulous. The rest of her exam was unremarkable. A head computed tomography (CT) scan without contrast was negative. An initial basic metabolic panel in the emergency room revealed sodium of 166 mmol/l, hence she was admitted to the intensive care unit (ICU). A complete blood count showed pancytopenia. A workup for hyponatremia was done and the results indicated central diabetes insipidus was the etiology. Patient was treated appropriately for DI and her hyponatremia improved with dextrose 5% in water (D5W) and DDAVP. Her sodium gradually improved. However, her mental status did not improve. An infectious disease consult was obtained to determine if an infectious etiology was the cause of her altered mental status. Magnetic resonance imaging (MRI) of the brain showed abnormal signals along the ependymal surface of the ventricular surfaces, which may indicate changes of ventriculitis. Hence, a lumbar puncture was done which was positive for cytomegalovirus (CMV) antigen. The CMV viral load in the CSF was found to be 3.9million copy/ml and the patient was started on ganciclovir. Clinically, the patient continued to have confusion and altered mental status. Foscarnet was added for concern for resistance to ganciclovir. She improved clinically after that and was discharged on oral ganciclovir. It was believed that the altered mental status was multifactorial secondary to hyponatremia as well as CMV encephalitis.

Discussion: It is not uncommon for immunocompromised patients to develop CMV infections and other complications. CMV infections involving hypothalamic and posterior pituitary structures are not well documented. However, a very rare and infrequently reported manifestation of CMV infection is central diabetes insipidus. We have found only one other case report of central DI associated with CMV infection in an immunocompromised patient. Clinicians should be aware of the CMV manifestations including the rare presentation of central DI. CMV has frequently been implicated and described in other endocrine dysfunction including the adrenals; however, it has not been demonstrated to infect the posterior pituitary gland. Recognizing the vast and even uncommon complications of CMV infection in immunocompromised hosts is imperative for a well-rounded clinical assessment.

A POTENTIALLY FATAL CHALLENGE, RULING OUT INFECTION IN IMMUNE MODIFIED PATIENTS

Tanner Jones, MS2

Introduction: While infection risk is widely publicized, diagnosing infection in patients prescribed high dose steroids and disease-modifying antirheumatic drugs (DMARDs) presents unique and underappreciated challenges. Abiding strictly by the SIRS criteria in this population is not sufficient and can result in patient harm since inflammatory processes are being suppressed. Additional advances are needed for making timely and proper diagnoses of infection in this population.

Case Description: a generally healthy 69 year-old male with an 18-year history of steroid-dependent rheumatoid arthritis (RA) presents with left wrist pain. Past medical history significant for left carpal tunnel repair/fusion, HTN, and having a bovine aortic valve. RA medications unchanged for past 8 years and consist of Remicade 600 mg and Solu-Cortef 250 mg every 8 weeks, Methotrexate 15 mg/weekly, and Medrol 2 mg b.i.d. Day 1. Sudden onset of pain and swelling in left wrist. ER work-up negative, showing only degenerative changes on X-ray. Patient given pain medication and recommended to follow-up with his rheumatologist. WBC 10.1, mild left shift, ESR 33. Blood cultures taken. Creat 1.2, BUN 35, PLT 187K. Day 2. Presents to the rheumatologist with severe left wrist pain and right foot/ankle swelling. The ER copy of the CBC was reviewed; rheumatology unaware of pending cultures. Wrist aspirate produces several drops of clear/blood tinged fluid. With no palpable warmth, patient diagnosed with an acute RA flare. Treated with a Depo-Medrol wrist injection, Medrol increased to 8 mg b.i.d., and Remicade infusion scheduled for the following day. Day 3. Presents for Remicade with an edematous and warm left wrist and right ankle. Using CBC from 36 hours prior, a septic process again ruled out. Day 4. The patient becomes lethargic and obtunded, is admitted to the ICU and started on empiric treatment for sepsis and probable meningitis. Both of the patient's previous blood cultures return positive for methicillin sensitive staph aureus and therapy for bacteremia quickly narrowed to Nafcillin. T 101, HR 115, RR 18, BP 95/62, WBC 14.3, Creat 2.8, BUN 62, PLT 79K, ESR 69, ALT 35, 56 WBCs in CSF- (95% polys). Day 6. CSF cultures grow MSSA. Creat 3.4, BUN 110, PLT 40K. Day 9. Having a poor prognosis and a DNR/DNI, the patient is transferred home under hospice care where he passes away on Day 10.

Discussion: Although repeatedly considered in this case, an infectious process was ruled out prior to patient developing CNS symptoms. Delayed diagnosis of infection led to higher steroid/DMARD dose, decreased response to antibiotics, and death. Revised guidelines and improved bacteremia testing are needed to help providers make timely and correct diagnosis of infection in the immune suppressed.

HYPERCALCEMIA INDUCED PANCREATITIS PRESENTING WITH ACUTE ST ELEVATIONS MIMICKING A MYOCARDIAL INFARCTION

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Introduction: New onset ST segment elevations with concurrent chest or epigastric pain typically indicate an acute coronary syndrome. ST segment elevations can also be seen in a number of other conditions, such as pericarditis, coronary vasospasm, or increased intracranial pressure (1). An uncommon, but increasingly cited cause of ST segment elevations is hypercalcemia. We report the first case of hypercalcemia induced pancreatitis presenting with ST segment elevations.

Case Description: A 32 year old male with poorly controlled diabetes presented with one day of vomiting and epigastric pain. On the night prior to presentation, the patient had multiple episodes of clear emesis. On the morning of presentation, he stopped vomiting, but developed acute onset of sharp, constant 7/10 pressure in the epigastric region that radiated to the back. An urgent care center EKG showed ST segment elevations for which he was sent to the Emergency Room.

Admission labs were significant for an elevated calcium of 17.0 mg/L in the setting of a normal albumin with creatinine of 1.4 mg/dL and lipase 296. Subsequently, an intact PTH was obtained, which was inappropriately normal at 40 pg/mL. Alcohol level, urine drug screen, D-dimer, Ionized Calcium, Vitamin D, and PTHrP were all within normal limits. Repeat EKG continued to demonstrate ST elevations. The patient was treated with aggressive IVF hydration and Calcitonin on admission. The patient's calcium level trended down to 9.8 mg/dL and his renal function normalized. The patient's EKG changes resolved with improvement in the calcium level and abdominal pain.

Discussion: 16 reported cases of hypercalcemia associated with ST segment elevations have been identified. (2-10) However, none of these reports were in the setting of acute pancreatitis. Hypercalcemia has been documented as a cause for acute pancreatitis due to the premature activation of trypsin, a pancreatic enzyme. (11) This patient's hypercalcemia was most likely from primary hyperparathyroidism due to the inappropriately normal PTH in the setting of an elevated calcium level. However the very high calcium level (above the average of 14.08 in primary hyperparathyroidism (10), indicates another factor was involved. The episodes of vomiting the night before the pancreatitis started likely caused the patient to become severely dehydrated and increased the calcium level.

Hypercalcemia is known to shorten the ST segment but the exact mechanism contributing to the ST elevation is unknown. While the ST segment elevations seem to mimic an acute myocardial infarction, on close inspection, a J wave can be seen. The presence of J waves is a subtle but important finding that has been associated with hypercalcemia. (3,4,9) In this patient, with ST segment elevations associated with a J wave, normal cardiac enzymes, and a normal TTE, consider hypercalcemia especially in the setting of pancreatitis.

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NOVEL ACVRL1 MUTATION IDENTIFIED IN LATE ONSET HEREDITARY HEMORRHAGIC TELANGIECTASIA

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Introduction: Hereditary Hemorrhagic Telangiectasia (HHT) is an autosomal dominant disorder with variable expressivity frequently presenting with recurrent epistaxis at adolescence. Here, we present a patient (pt) with a rare, late-onset disease course featuring a novel mutation in ACVRL1, a signal transducer in the TGF β /BMP pathway.

Case: 62 yo female who presented 08/26/15 with worsening episodic epistaxis, fatigue, dyspnea on exertion for 10 years. Physical exam revealed 1mm cherry red macules on the tongue surface along with telangiectasias of the extremities. Labs: HGB 9.4 g/dL (low), HCT 30.1% (low), MCV 78.7 fL (low), RDW 23% (high), Reticulocytes 112700 cells/uL (high), Ferritin 17 ng/mL (low). CMP, PT, PTT, & fibrinogen were normal. Fiberoptic examination by otolaryngology revealed multiple telangiectasias in the nasal mucosa. CT chest abdomen and pelvis 10/1/14 lacked well-defined AV malformations. Targeted sequencing of the exons and exon-intron junctions of known HHT genes, ENG, ACVRL1, SMAD4, RASA1 and BMP9, returned a previously unreported missense mutation in ACVRL1, resulting in a c.998G>A nucleotide substitution and p. Ser333Asn amino acid alteration. The patient was a heterozygote for this alteration. Her final diagnosis is microcytic anemia due to chronic blood loss due to HHT related epistaxis. She was treated with oral iron and periodic ENT cauterizations with stabilization of symptoms and HGB (11.9 g/dL, 9/2/15).

Discussion: Here we have a late-onset variation of HHT in the presence of a novel, suspected pathogenic mutation in ACVRL1. HHT patients typically present with recurrent nosebleeds by the age of 30 (90%), superficial telangiectasias by the age of 40 (67%) and GI bleeding starting in their 50s. This patient reported recurrent epistaxis onset in her late middle age and at the age of 62 does not complain of GI bleeds. Abdominal and chest CT revealed an absence of visceral AVMs. A mutation occurring at the same nucleotide position, c.998, but resulting in a different amino acid change, has been found in multiple other HHT patients. The clinical presentation of these patients is unknown, however the presentation of our patient suggests a c.998G>A missense mutation causes a late-onset HHT clinical presentation managed with supportive care.

SPLENIC ARTERY ANEURYSM – THE FORGOTTEN COMPLICATION OF CIRRHOSIS

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Splenic artery aneurysms (SAA) are rare overall but more common in pregnancy and patients with cirrhosis. Although the risk of rupture is low, the mortality rate once ruptured is high. The treatment options require a facility with advanced resources, underlying the need for prompt diagnosis.

A 53-year-old female with Child-Pugh class C cirrhosis secondary to alcohol abuse presented with two days of sudden onset 9/10 abdominal pain and weakness without other symptoms. She was hypotensive at 82/57mmHG with mild tachycardia to 96bpm and a new O2 requirement of 2L. Her hemoglobin and hematocrit dropped from 9.8/29 to 7.3/22 in 3 hours. Computed Tomography (CT) of the abdomen and pelvis using contrast showed a large left intraperitoneal hematoma with active extravasation from a probable ruptured SAA. She received two units of packed red blood cells before being transferred to the University of New Mexico Hospital. Upon arrival she underwent emergent splenic artery embolization by Interventional Radiology (IR) without complication. She was discharged home on day five but re-presented five days later with worsening abdominal pain. CT showed a large hematoma and hemoperitoneum with active bleeding originating near the previously embolized SAA that was consistent with a re-bleed. The patient was determined to be a poor surgical candidate due to coagulopathy, liver failure, and poor nutrition. Moreover she was clinically stable so surgical intervention was not indicated. She was admitted to the medicine service until discharge to an inpatient rehabilitation center.

Pre-2000 literature reports an incidence of 7-17% in patients with cirrhosis, however that number is likely higher now due to increased incidental detection on imaging. The proposed mechanism in patients with cirrhosis is increased splenic blood flow in response to portosystemic shunts. SAA is a complication of liver transplant and most reports are in surgery and transplant journals, leading to a paucity of information available for general internists. Interventional options consist of splenic artery ligation, coil embolization, or splenectomy. The risk of rupture is low, only 2-10% in older literature and likely even lower due to increased incidental detection in asymptomatic patients, but the mortality rate of ruptured aneurysms is 29-36%. Despite the rarity of SAA, due to its high mortality rate and need for specialized intervention we recommend that physicians consider SAA in their differential diagnoses for abdominal pain, particularly in patients with cirrhosis.

REFRACTORY HYPOPHOSPHATEMIA IN SUNNY NEW MEXICO

Arianna Pregenzer-Wenzler, Emily L. Hanson, MD, Jacob G. Imber, MD

Hypophosphatemia can have multiple etiologies, and in a hospitalized patient it is not an electrolyte abnormality that normally warrants much concern. However, severe, refractory hypophosphatemia is much less common and may be the only sign of a more serious underlying deficiency.

A 43-year-old woman with a history of alcohol dependence presented to the emergency department with severe right upper quadrant (RUQ) pain, nausea and fever. She was admitted to the Medical ICU for septic shock secondary to cholangitis complicated by acute alcoholic hepatitis. Once stabilized, the patient was transferred to the floor for management of her acute conditions.

At time of transfer the patient was afebrile with persistent nausea and RUQ pain. She was alert, oriented and answering questions appropriately. Physical exam showed scleral icterus, jaundice and scattered spider angiomas. Her abdomen was moderately distended and painful to palpation in the RUQ. Hepatomegaly was appreciated. Labs were notable for leukocytosis, transaminitis, hypoalbuminemia and multiple electrolyte abnormalities including hypokalemia, hypomagnesemia, hypophosphatemia and hypocalcemia. The patient's corrected serum calcium was within normal limits and her renal function was normal.

The patient's electrolytes were repleted but a chemistry panel the next morning was significant for critically low phosphorus at 0.7 mg/dL. Her phosphorus was again replaced, and her serum phosphorus showed a transient response. Over the next few days, the patient's phosphorus continued to decline, reaching a nadir of 0.1 mg/dL despite aggressive replacement. Aside from mild irritability, the patient remained asymptomatic, denying bone pain or muscle weakness.

Further work up revealed a parathyroid hormone level of 176 with a low ionized calcium, indicating secondary hyperparathyroidism concerning for vitamin D deficiency given her normal renal function. The patient was started on calcium replacement and a standard over-the-counter dose of vitamin D. Five days later, when her 25,OH vitamin D level returned measuring undetectably low, treatment with Ergocalciferol 50,000 IU twice weekly for six weeks was initiated. Once three treatments with high-dose vitamin D were given, the patient's serum calcium and phosphorus levels began to stabilize.

Severe vitamin D deficiency, leading to refractory hypophosphatemia is an uncommon diagnosis in the inpatient setting of New Mexico, where the sun shines 300 days of the year. In the setting of generalized electrolyte deficiencies, this patient's low phosphorus levels were initially considered to be secondary to poor oral intake, refeeding syndrome, alcoholism and alcohol withdrawal. However, the severe, refractory nature of her hypophosphatemia prompted a more complete workup. This case illustrates the importance of considering vitamin D deficiency in the patient with refractory hypophosphatemia, as low phosphorus levels may be the first, subtle sign that a deficiency is present.

LEVAMISOLE-COCAINE INDUCED AGRANULOCYTOSIS

Adam Johnson

Introduction: Severe insidious agranulocytosis can be a cause for alarm and can have many etiologies. When a patient presents with signs and symptoms of immunodeficiency, drug use may be on the differential. Cocaine laced with the veterinary anti-helminthic agent, levamisole, has a rare side effect of severe agranulocytosis. It is important for health care workers to be aware of this cause of extreme agranulocytosis so we can treat effectively and educate on its dangers.

Case: A 30 y.o. female presents to the ER with sore throat, mucous stools approx. 20 times daily, 30lb unintentional weight loss and tactile fever at home. Other symptoms include headaches, fatigue, cough and myalgias. These symptoms had been reported as gradually getting worse over the last 2 weeks. Patient later mentions h/o regular cocaine use, most recent 5 days ago and seen 1 month ago for herpetic lesions to lips. On Review of systems, no chest pain, shortness of breath, abdominal pain, or rash. Physical examination showed an ill appearing patient with dry, erythematous oropharynx, scabbed herpetic lesions to left oral commissure, anterior cervical lymphadenopathy, tachycardia, and decreased breath sounds. Initial work-up showed HIV negative, CXR negative, EKG with no acute ST-T wave changes, NSR, throat culture negative for strep, WBC of 0.8 ($\times 10^3/\text{UL}$) and UA positive for cocaine and eventually levamisole. Normal WBC is between 4.0 and 10. Patient was given a course of 1 g IVPM Vancomycin, 1g and 2 g IVPM Cefepime, 300mcg injection Filgrastim and 100mg and 200mg Fluconazole tablets over the course of her 35 day hospital stay.

Discussion: Before levamisole was first withdrawn from markets in 1999, it was used as an anti-helminthic agent in humans and mostly animals. Possibly due to levamisole's similar chemical properties, it was found by the DEA to be cut with more than 80% of seized cocaine in 2011. The dangers of levamisole are that it can cause agranulocytosis and also vasculitis, or, 'levamisole induced necrosis syndrome', where the patient presents with erythematous painful papules anywhere on the skin. It is interesting and still unexplained why many patients test positive for levamisole but very few, less than 5% of the studied population, experience serious illness. In the case of our patient, she suffered severe agranulocytosis and recovered almost immediately upon stopping her drug use and starting medications. Within 24hours her WBC was at 3.8 and 9.5 by discharge. There are several articles detailing the few recorded cases of patients that used cocaine or crack cocaine that presented in an immunocompromised state. With the knowledge of adulterated cocaine we can be aware of other etiologies of agranulocytosis, we can rapidly alleviate patient symptoms and improve healthcare through the education of the dangers of drug use.

A STIFF DRINK

Ian Kratzke

A 51 year old male was brought to the ED by his sister after a night of profuse vomiting. His affect was blunted and he said that he regretted it. What “it” was, he wasn’t ready to say. He was hypertensive but not in acute distress. Physical exam showed no pertinent positives. IV’s were placed, fluids were given and blood was taken. He was found to have an anion gap of 35 and an arterial pH of 7.34. The mnemonic “MUDPILES” for High Anion Gap Metabolic Acidosis (HAGMA) likely went through the resident’s head. His serum osmolality was found to be 307, which was 14 more than the calculated osmolality of 293. This gap indicated that something else unmeasured was in his blood. These findings led the medical team to a most likely scenario, that this man drank ethylene glycol.

The fomepizol was prepared, which would competitively bind the alcohol dehydrogenase enzyme that was currently metabolizing the less toxic ethylene glycol in his body down the pathway to the very toxic glycolate and oxalic acid. As the team began to explain to the patient their treatment plan, he finally revealed his story: he had been suffering from progressive insomnia and depression due to the stress of caring for his mother with dementia. As his mental health deteriorated, so did his social life and his partner ended their relationship. He decided to end his life.

He found the anti-freeze and tried to drink the 32 ounces he had in his garage. However, he was scared and wanted to calm his nerves first, so he drank half a bottle of whiskey, which unwittingly acted much like the fomepizol and bound up the metabolizing enzymes, keeping most of the ethylene glycol from being converted to its toxic form. He went to bed hoping to never wake up, but early in the night, after repeated episodes of uncontrollable vomiting, he decided to reach out to his sister for help.

During his hospital stay, he was given over 10 rounds of hemodialysis to clear the toxin and temporarily replace his kidneys, as his serum creatinine rose to over 12 with an estimated GFR of 5. He remained anuric for 2 weeks. Over time, the AKI resolved and his physical state improved, as did his mental health and will to live.

Ethylene glycol is widely available, affordable and apparently tolerable to the taste buds. While fomepizole should be the standard treatment, ethanol may serve as a temporary replacement when necessary. Its textbook presentation and effects, commonly used as a teaching point for metabolic acidosis, are readily applicable to real-life clinical scenarios, and timely application of this knowledge may save lives.

ATYPICAL PRESENTATION OF SARCOIDOSIS MIMICKING LYMPHOMA

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While the majority of sarcoidosis cases present primarily with pulmonary involvement, some patients exhibit predominantly extra-pulmonary manifestations. Other diseases which may present similarly need to be excluded, often necessitating histopathologic detection of non-caseating granulomas before the definitive diagnosis can be given.

A 34-year old African-American male presented with six months of fevers, self-reported 23 kg weight loss, night sweats, dyspnea on exertion, and non-productive cough. This was followed by two months of worsening abdominal pain and distension. He was a former cigarette smoker, current marijuana smoker, born and lived in New York, and had never traveled outside of the US. The physical exam was notable for tachycardia, pruritic maculopapular lesions scattered on tattooed extensor surface of his arms, and inguinal lymphadenopathy. He had crackles at bilateral upper lung fields, and breath sounds were diminished at bilateral lung bases. Abdominal examination revealed tenderness in both the right and left upper quadrants and significant hepatosplenomegaly with liver edge palpable 14 cm below the right costal margin and spleen palpable 12 cm below the left costal margin. His labs were notable for white blood cell count 10.6 k/uL, hemoglobin 11.2 g/dL, elevated immunoglobulins (IgA 750 mg/dL, IgG 3230 mg/dL), albumin 2.9 g/dL, total protein 9.7 g/dL, AST 64 U/L, ALT 70 U/L, alkaline phosphatase 1184 U/L, LDH 704 U/L, negative QuantiFERON, negative HIV screen, and proteinuria of 30 mg/dL. A CT scan of the chest, abdomen and pelvis showed heterogeneous hepatosplenomegaly and peritoneal, mediastinal and retroperitoneal lymphadenopathy. Lymphoma was suspected. The results of a CT-guided needle core biopsy of a retroperitoneal lymph node showed virtually complete replacement of normal architecture due to infiltration by non-necrotizing non-caseating epithelioid granulomata. Flow cytometry revealed immunophenotypically unremarkable B and T cells with no immunophenotypic evidence of non-Hodgkin lymphoma. Tissue gram stain, fungal culture and AFB cultures were also negative. A punch biopsy of a tattoo papule further revealed non-caseating granulomas, consistent with a diagnosis of sarcoidosis. Prednisone therapy was initiated with improvement of most of his symptoms, although abdominal distension and pain persisted.

This case demonstrates the challenge in diagnosing sarcoidosis in the absence of classic pulmonary findings due to the potential similarity in presentation to lymphoproliferative diseases and infections like non-pulmonary tuberculosis. Sarcoidosis is a diagnosis of exclusion. In order to diagnose sarcoidosis, a patient requires having clinical evidence of sarcoidosis such as radiographic findings and/or clinical symptoms consistent with sarcoidosis. Sarcoidosis can involve any organ system, and clinical presentation varies depending on the specific organ involved. Sarcoidosis can present with B symptoms (fever, night sweats and weight loss), mimicking lymphoma without the classic pulmonary manifestation. If a patient presented with such symptoms, sarcoidosis should be included in the differential diagnosis until biopsy proven otherwise.

ACUTE HEART BLOCK IN A MEDICAL STUDENT

First Author: Hamza Murtaza

Lyme disease is a tick-borne illness reaching epidemic proportions in the Northeast. Atypical presentation of the disease can be a diagnostic challenge.

I, a 25-year old male, with no significant medical history, reported to the student health center with abdominal pain, fatigue upon exertion, and general malaise. Vital signs were stable except for an irregular pulse in the lower 30s. A physical examination of the abdomen was negative for distension, organomegaly, and tenderness. Since I had been fasting during daylight for the previous two weeks, an electrolyte imbalance was predicted. Blood work, abdominal x-ray, and an electrocardiogram were ordered. Blood tests returned, normal ruling out an electrolyte imbalance, and the abdominal x-ray revealed mild constipation. But, the electrocardiogram, performed the following day, showed a complete heart block. I was immediately transferred to the emergency department. Two weeks prior to my initial presentation, I experienced pain in my left shoulder, which I had attributed to exercise soreness or ill-postured sleeping. At the same time, I felt severe left jaw pain and orthostatic hypotension. Both the shoulder and jaw pain resolved within a few days. However, orthostatic hypotension progressively worsened and minor exertion became increasingly difficult. In the emergency room, I shared a family history of HOCM, upon which an echocardiogram was performed. It was negative for any structural abnormalities. With further investigation of my medical history, I told the team about my recent trip to Acadia National Park in Maine. Suddenly, a vector-transmitted disease became high on the differential. I was started on ceftriaxone intravenously. Meanwhile, a temporary trans-venous pacemaker was placed, and I was admitted to the cardiac intensive care unit. Although there was an absence of a tick bite or rash on my body, the team strongly suspected Lyme carditis to be the cause of my presentation. PCR and western blot tests came back positive for Lyme disease. Over the next few days, my heart rate began to improve, and I became independent of the pacemaker in 6 days. I was discharged the following day with PICC line and ceftriaxone for 21 days.

Of the 30,000 Lyme cases reported each year, only 1% present with meningitis or Lyme carditis. My case elucidates the value of a complete history and demonstrates that a lack of the hallmark rash can often lead to the underestimation of symptoms. Although Lyme carditis is relatively rare, proper recognition is imperative for treatment as complications can be fatal.

SERONEGATIVE LYME MENINGITIS: A CASE REPORT

First Author: Kevin Wong Mentor: Nikolaos Mavrogiorgos

Introduction: Lyme disease is the most common vector-borne disease in the United States and is defined by 3 stages, each with distinct clinical features. Given its frequency and characteristic features, physicians in endemic regions are usually successful at identifying cases of Lyme disease. In this study, we report a patient with an atypical presentation of Lyme meningitis.

Case: A 19-year-old female from Massachusetts with no significant past medical history presents to the hospital with fever and malaise. Review of systems was negative for headache, tick bites, rash, joint pain, or arrhythmias. Lymph nodes and cranial nerves were also normal on physical exam. The patient was sent home with a diagnosis of bronchitis but returned three days later for unimproved symptoms. On chest radiograph, infiltrates were noted in the right lung so the patient was diagnosed with uncomplicated community acquired pneumonia and sent home with antibiotics. Three days later, the patient returned for the third time with new-onset frontal headaches. Urinalysis, blood cultures, and sputum cultures were all negative. Initial cerebrospinal fluid (CSF) analysis yielded neutrophilic pleocytosis with a WBC count of 600 cmm, with 39% neutrophils, 55% lymphocytes and 6% monocytes. CSF protein was elevated and glucose was low. ELISA and Western Blot for Lyme in the serum were both negative. Enzyme immunoassay (EIA) for CSF Lyme antibodies was also ordered but results were pending. The patient was started on acyclovir and ceftriaxone and symptoms of headache and fever greatly improved over the next few days. Acyclovir was stopped when the HSV PCR in the CSF came back negative. A second CSF sample obtained five days later yielded improved findings of 60 cmm WBCs. After 7 days of antibiotics, the patient was discharged from the hospital. One day later, the EIA came back positive for Lyme IgM in the CSF so the patient was called back for treatment with IV ceftriaxone for two weeks.

Discussion: This case of Lyme meningitis has several atypical characteristics. Firstly, the negative Lyme serology in this patient was highly unusual. Serologic testing for antibodies to *B. burgdorferi* is very sensitive and specific, with detection rates over 95% for Lyme meningitis. Additionally, unlike other CNS infections, Lyme meningitis does not present with CSF leukocytosis, however, this patient's CSF studies showed lymphocytic pleocytosis as well as elevated neutrophils. Altogether, these findings together with the noncontributory history and physical made this an especially challenging case.

Conclusion: We report an unusual case of Lyme meningitis that not only presents with atypical CSF characteristics, but also negative serology. Physicians in endemic regions should always maintain a high index of suspicion in patients presenting with meningitis.

VENTRICULAR ASSIST DEVICE IMPLANTATION IN A PATIENT WITH DEEP BRAIN STIMULATOR

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Introduction: As life expectancy is increasing, and survival of myocardial infarction is improving, the heart failure patient population is expanding. With a discrete number of hearts available each year for transplantation, options for mechanical therapy such as left ventricular assist devices (LVAD) have become increasingly relevant. There are no current nationally accepted guidelines to assist physicians in patient selection for these devices. Generally accepted roles for LVAD implantation include those for destination therapy as well as those as a bridge to cardiac transplantation. With improvements in these devices over time, previous limitations related to body habitus and comorbidities have become less prohibitive. Accordingly, broader groups of individuals are being considered for this therapy, even those with significant non-cardiac medical history.

Case: We present the case of a 71 year-old African American female with a past medical history notable for a medically-refractory essential tremor for which she underwent staged bilateral deep brain stimulator (DBS) implantation five years prior. She had non-ischemic dilated cardiomyopathy, status post implantable cardioverter defibrillator (ICD) placement who presented with New York Heart Association Class 4 symptoms, despite more than 6 months of optimal medical therapy. Her echocardiogram revealed severe global hypokinesis of the left ventricle with an ejection fraction of 15%. Right heart cardiac catheterization revealed a cardiac output of 3.7 liters per minute and cardiac index of 1.71 liters per minute per square meter via the thermodilution method. There was much debate regarding the safety of LVAD implantation in this individual because of her DBS, particularly with the need for cardiopulmonary bypass, but ultimately the decision was made to insert a Thoratec Heartmate II device as destination therapy. Her peri-procedural course was uncomplicated. In addition, she had successful bilateral DBS generator replacement within a year of the LVAD placement without interruption of systemic anticoagulation. Overall, her functional status has significantly improved as a result of the LVAD.

Discussion: This case illustrates the potential for severe heart failure patients with multiple co-morbidities and implantable devices, such as DBS, to undergo successful LVAD placement. To date, there are no easily identifiable case reports of patients with DBS undergoing LVAD placement. The safety and efficacy of LVAD implantation in such patients has not yet been fully evaluated. Thus, cases such as this are essential in defining possibilities for therapy in similar patients.

THE PRESSING CASE OF BLUE FINGERS AND DEPIGMENTED SKIN

Kun Wei Song, BA Laura W. Musselwhite, MD, MPH David Ming, MD Rebecca E. Sadun, MD, PhD

Introduction: Long-standing rheumatologic diseases frequently affect the central nervous system (CNS), but CNS manifestations are rarely the presenting symptom. Posterior reversible encephalopathy syndrome (PRES) is a brain disorder characterized by headaches, altered consciousness, visual disturbances, and seizures. PRES is most commonly associated with hypertensive encephalopathy, eclampsia, and use of immunomodulatory drugs. Although PRES is an uncommon presentation of rheumatologic disease, it has been observed in both systemic sclerosis and lupus.

Case Report: A 51-year-old African-American female, with no significant past medical history, presented with a 2-week history of headaches. She was admitted for hypertensive crisis with a blood pressure of 240/113. Subsequently, she experienced a generalized tonic-clonic seizure, acute encephalopathy, and left-sided hemiplegia. Her brain T2 MRI showed posterior hyperintensity concerning for rhomboencephalitis. As her blood pressure improved over the next 48 hours with antihypertensive therapy, her left-sided hemiplegia resolved and mental status normalized. Neurologic work-up was negative for infectious and vascular causes and she was diagnosed with an atypical presentation of PRES.

On admission, her physical exam revealed Raynaud's phenomenon, a telangiectasia on her lip, and vitiligo on her arms. As her mentation improved, additional history revealed years of dysphagia and a family history of rheumatoid arthritis. A rheumatologic evaluation revealed an ANA of 1:2560 and elevated levels of multiple autoantibodies. These included a +anti-Sm, +anti-RNP (336 IU/ml by Luminex multiplex; normal <100 IU/ml), +anti-Ro, -anti-La, +anti-centromere antibody, -anti-Scl-70, -anti-RNA polymerase III, -dsDNA, +anti-CCP antibody, and +RF. Additional evaluation included a transthoracic echocardiogram (normal) and urinalysis (normal), while her CBC was remarkable for lymphopenia. Her clinical presentation included features of both lupus and limited systemic sclerosis, but did not meet full diagnostic criteria for either. In the context of the clinical presentation and significantly elevated anti-RNP, she was diagnosed with MCTD and started on hydroxychloroquine. She was later discharged following normalization of her blood pressure and mental status.

Discussion: Immunosuppressive therapy is a known risk factor for PRES, but autoimmune diseases themselves present a less clear link. PRES associated with rheumatologic diseases such as lupus has been described in case reports, but neither the mechanism nor the epidemiology have been elucidated. This case underscores several significant clinical points: 1) PRES can be the initial presenting symptom of rheumatologic disease, 2) elusive rheumatologic diagnoses can be identified through careful physical exam and review of systems, and 3) consider PRES in cases of suspected autoimmune disease and concurrent neurological dysfunction. PRES is an important entity to identify because early diagnosis and treatment of the underlying etiology offers the best chance of full neurologic recovery.

IT'S NOT BREAST CANCER? A CASE OF POEMS SYNDROME MASQUERADING AS METASTATIC CANCER WITH UNKNOWN PRIMARY

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Case presentation: A 40 year old woman with history of stroke at age 35 was admitted from an outside hospital with a CT-PE scan showing diffuse “osteoblastic” lesions and bilateral axillary lymphadenopathy. She complained of progressive weakness and painful paresthesias in her upper and lower extremities, diffuse body swelling, and a 100-lb weight loss all within the past year. On exam, she had motor and sensory deficits, anasarca, hirsutism affecting her face and extremities, skin hyperpigmentation, and peau d’orange changes in both breasts without palpable masses. Workup for metastatic breast cancer was initiated, but bilateral mammograms were negative and her bony lesions were not metabolically active on PET/CT scan. Part of her neuropathy workup included an SPEP, which showed a small IgG lambda spike of 0.4 g/dL. EMG showed a demyelinating polyneuropathy. Eye exam showed bilateral papilledema. VEGF was slightly elevated at 87 pg/mL. Bone marrow biopsy showed a clonal lambda plasma cell population. This patient was discharged with a diagnosis of POEMS syndrome. She received an autologous stem cell transplant and her neuropathy and edema gradually improved.

Discussion: POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal paraprotein, skin changes) syndrome is a rare plasma cell dyscrasia. Additional features include sclerotic bony lesions, extravascular volume overload, papilledema, elevated VEGF, and risk of thrombosis. The pathophysiology is poorly understood but symptoms are thought to stem from cytokine secretion. The diagnosis of POEMS syndrome is easily missed due to its complexity and rarity. The osteosclerotic lesions can be confused for blastic metastases from underlying solid malignancy, and the neuropathy presents similar to that of chronic inflammatory demyelinating polyneuropathy. The standard of therapy for diffuse disease without significant organ dysfunction is autologous stem cell transplant (ASCT). Progression free and overall survival 5 years after ASCT is 75% and 94% respectively.

Conclusions: A patient with underlying POEMS syndrome represents a significant diagnostic challenge in the inpatient setting. Hospitalists may be the first to encounter such a patient and must recognize the importance of unifying the seemingly unrelated symptoms. Furthermore, they should keep an open mind when evaluating patients with metastatic bone disease; POEMS syndrome should be on the differential when a patient presents with osteosclerotic lesions without primary solid tumor, polyneuropathy, and a positive SPEP with lambda M spike.

CARDIOGENIC SHOCK SECONDARY TO THYROID REPLACEMENT

First Author: JOYCE NJORGE Mahmoud Farhoud, MD Chantal ElAmm, MD

Introduction: Dilated cardiomyopathy (DCM) is defined as the dilation and impaired function of the ventricles diagnosed on imaging. Endocrinopathies are common causes of secondary dilated cardiomyopathy. There are multiple cases of cardiomyopathy detected in hypothyroid patients reversing with levothyroxine treatment. There are few papers describing the rapid correction of hypothyroidism resulting in cardiac injuries but, to our knowledge, there are no case reports of cardiomyopathy and cardiogenic shock after intravenous levothyroxine.

We report the case of a patient presenting in the setting of recently diagnosed hashimoto thyroiditis whose heart function rapidly declined after initiation of levothyroxine treatment

Case Description: A 39 year-old woman presented to the ED complaining of two weeks of profound weakness. Physical exam was grossly normal. Vital signs were notable for bradycardia of 53 BPM. Her TSH was found to be elevated at 287 mIU/mL and free T4 decreased at 0.15 ng/dL. An echocardiogram demonstrated a normal ejection fraction of 55-60% without valvular or pericardial abnormalities. She was diagnosed with Hashimoto thyroiditis and treated with IV and PO levothyroxine and was discharged on PO levothyroxine and prednisone with outpatient follow-up.

One month later, she returned to the ED complaining of worsened shortness of breath since discharge and one episode of waking up with severe difficulty breathing. Her vital signs were significant for sinus tachycardia. Physical exam was significant for jugular venous distention and summation gallop with diminished lung sounds bilaterally. Her echocardiogram showed an ejection fraction of 20% with left ventricular systolic dysfunction. Her TSH was 19.4 uIU/mL with elevated anti-TPO antibodies of 50IU/m. Coronary catheterization demonstrated non-obstructive coronary artery disease and decompensated hemodynamics. A right heart catheterization demonstrated elevated right atrial, pulmonary arterial, and wedge pressures.

She was vasodilated with IV nitroprusside then transitioned to oral vasodilators and a guideline derived heart failure regimen consisting of beta blockers and diuretics. Cardiac MRI done at time of discharge demonstrated globally mildly decreased systolic function with an LVEF improved to 47%. Echocardiography one month after discharge demonstrated normal left ventricular systolic function with an estimated LVEF of 55-60%. At this point, she was therapeutic on 75 mcg levothyroxine (TSH of 0.08 uIU/mL) and did not have further complaints of dyspnea or fatigue

Discussion: Known for their function in maintaining and affecting basal metabolic rate, thyroid hormones also have significant effects on cardiovascular dynamics. Hyperthyroid states increase the risk of cardiovascular disease and dysfunction because of induction of a high-output state. Therefore, it is important to keep this concept in mind while initiation treatment with levothyroxine. Thyroid replacement is becoming more common because of increased screening for thyroid disease in the primary care setting. We present this case as evidence of the importance of considering treatment regimens (dosage, frequency, and administration route) for endocrinopathies, especially

those involving thyroid hormone, a ubiquitous hormone with widespread effects. In addition, cardiac function should be regularly evaluated during the course of hormone replacement therapy.

STREPTOCOCCUS DYSGALACTIAE SUBSPECIES EQUISIMILIS BACTEREMIA COMPLICATED BY SEPTIC EMBOLI IN THE BRAIN

Lei Lei, Modi Rohan, Vijay Duggirala (Ohio State Medical Center, Columbus, OH)

INTRO: *Streptococcus dysgalactiae* subspecies *equisimilis* (SDSE) is a group of commensal bacteria whose pathogenic potential has gradually gained attention. A high index of suspicion is needed for the recognition of serious complications associated with SDSE bacteremia.

CASE DESCRIPTION: 76 y.o female with a history of ER/PR +Her2-breast cancer, aortic stenosis, and hypertension presented with fever, chills, and painful swelling of incision site status post right sided mastectomy. Broad spectrum antibiotics were initiated. Peripheral blood cultures grew pan-sensitive strep equisimilis while the urine culture grew pan-sensitive *E. Coli*. Cellulitis and SDSE bacteremia resolved within three days. Thus the patient was transitioned to ceftriaxone to complete a two-week course of antibiotics.

Several days later the patient had an episode of transient left facial droop, left arm and leg weakness, and slurred speech. MRI and CTA of brain demonstrated acute embolic stroke without hemorrhage in the right superior MCA territory. Physical exam was without neurological deficits and was significant for a grade 3 systolic ejection murmur. Transesophageal echocardiogram revealed a 1.5 cm x 0.9 cm mobile calcified mass on the mitral valve concerning for vegetation. Repeat blood cultures were negative and patient was started immediately on continuous high dose IV penicillin, remaining symptom free for the remainder of her hospital course. Repeat TEE one week later re-demonstrated calcified valvular mass of stable size. Per Infectious Disease, the patient was discharged home on IV penicillin to complete a four-week antibiotic course.

DISCUSSION: SDSE originates from endogenous or exogenous sources¹. Animal contact is implicated in 24% of the cases, which is relevant to our patient who had close contact with her granddaughter, an avid horseback rider^{2,3}. Moreover, this infection can cause arthritis, bacteremia, cellulitis, and pharyngitis and is often seen in elderly patients with heart disease, diabetes, malignancy or immunosuppression¹. Previously documented complications with SDSE include respiratory distress and toxic shock syndrome^{1,4}. This case illustrates how rapid clearance of SDSE bacteremia does not preclude the development of serious complications, such as endocarditis and embolic stroke.

Reference:

¹ Sinner SW, Tunkel AR. Viridans Streptococci, Nutritionally Variant Streptococci, Groups C and G Streptococci, and Other Related Organisms. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (8th ED) 2015. 2349-2361.

² Bradley SF, et al. Group C streptococcal bacteremia: analysis of 88 cases. Rev. Infect. Dis 1991, 13 (2): 270-80.

³ Brouwer MC, et al. A horse bite to remember. Lancet 2010, 376 (9747):1194.

⁴ Takahashi, et al. Clinical aspects of invasive infection with *Streptococcus dysgalactiae* subsp. *equisimilis* in elderly patients. J Infect Chemother 2010, 16(1): 68-71.

DOXYCYCLINE INDUCED PANCREATITIS

First Author: Nahid Rashid

INTRODUCTION: Drug-induced pancreatitis is the third leading cause of pancreatitis following alcohol abuse and gallstones. Over 525 drugs have been suspected to cause pancreatitis. Many of these drugs are commonly used and include antibiotics, antihypertensives, chemotherapeutic drugs, anti-virals and NSAIDs. The majority of these drugs were identified through case reports. There have been three large reviews that used case report summaries to categorize drugs as definite or probable causes of pancreatitis and doxycycline is reported to be a probable cause. This vignette identifies a patient with a presentation supportive of doxycycline-induced pancreatitis given the timeline of his presentation and lack of other clear etiology.

CASE REPORT: A 64-year-old male presented to a tertiary care center the day he returned from a trip to Haiti with one week of progressive abdominal pain, nausea and vomiting, and altered mental status. The abdominal pain was diffuse but worse in the umbilical region with radiation through to his back. The pain and nausea with vomiting coincided with the initiation of doxycycline 250 mg daily for malaria prophylaxis. The patient received a total of four doses of doxycycline but self-discontinued due to nausea and vomiting. He denied a history of gallstones, significant alcohol use, or prior history of pancreatitis.

Labs on admission were significant for serum lipase 1092 (reference range: 23-300), normal liver function tests, leukocytosis to 14.7, and a creatinine of 14.87 with a baseline of 1. Computed tomography of the abdomen/pelvis showed presence of non-obstructing cholelithiasis, and no evidence of duct dilation or cholecystitis. Triglyceride level was normal. Intrinsic and obstructive causes of acute kidney injury were evaluated and unrevealing. The patient was managed with bowel rest and aggressive IV fluid resuscitation. His abdominal pain and altered mental status resolved rather quickly, and he went on to have complete resolution of acute kidney injury.

DISCUSSION: Pancreatitis is a dangerous adverse reaction of commonly used drugs, with up to 10-30% mortality. Although it is rare, drug-induced pancreatitis is now considered to be the third leading cause of pancreatitis. Up to 5.3% of cases of pancreatitis are determined to be drug-induced, however this number may be considerably higher as it is a difficult diagnosis to confirm. It is important to consider drug-induced causes for all patients that develop pancreatitis without any of the common risk factors. This is especially true with a history of newly initiated medication.

Currently there are four reported cases of doxycycline-induced pancreatitis. This case is presented to increase awareness and further the evidence of doxycycline-induced pancreatitis, which is currently considered a probable cause of pancreatitis according to the Netherlands Centre for monitoring adverse reactions to drugs.

EPSTEIN-BARR VIRUS-INDUCED MACROPHAGE ACTIVATION SYNDROME IN THE SETTING OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

Catherine D. Zhang, James P. Dugan, Stacy P. Ardoin

INTRODUCTION: Macrophage activation syndrome (MAS) is a severe, potentially fatal complication of rheumatic diseases that can be triggered by infections, modifications in drug therapy, or during periods of high rheumatic disease activity. The pathophysiology is characterized by the excessive activation of hemophagocytic macrophages and T lymphocytes leading to an overwhelming inflammatory state. MAS bears close similarity to hemophagocytic lymphohistiocytosis (HLH) and is often classified among secondary or reactive forms of HLH.

CASE: A 19 year old female with a history of systemic juvenile idiopathic arthritis (SJIA), on monthly canakinumab, presented with high fever, fatigue, myalgias, and mild abdominal pain. She was febrile to 103.3 degrees F with prominent cervical lymphadenopathy on physical exam. No synovitis, rash, or hepatosplenomegaly was noted. Initial laboratory studies were remarkable for pancytopenia and transaminitis. Infectious cultures and serologies were negative except for a high Epstein-Barr virus (EBV) viral load. The diagnosis of MAS was made when further studies revealed hyperferritinemia (25,650 ng/ml), low ESR (3 mm/hr), hypofibrinogenemia (181mg/dl), and elevated soluble IL-2 receptor level (2814 U/mL). Based on these findings, she was started on methylprednisolone 1 g/day with resolution of her fevers and gradual improvement of her cytopenias, liver chemistries, and ferritin level over the next several days. She was discharged home on dexamethasone with close follow up, but was readmitted two weeks later with return of high fevers, pancytopenia, worsening transaminitis (ALT/AST: 1462/1255 U/L) and hyperferritinemia (46,757 ng/ml), as well as a marked increase in EBV titer from 32,091 viral copies/ml to 222,782 copies/ml. The patient was again started on methylprednisolone 1 g/day with the addition of cyclosporine 3mg/kg on hospital day 3. At the time of discharge, her fevers were resolved and EBV viremia and laboratory markers improving. Of note, a bone marrow biopsy to assess for evidence of hemophagocytosis was not performed since these findings would not have altered management. A HLH genetic panel to assess for underlying genetic propensities for MAS was negative.

DISCUSSION: While MAS can complicate almost any rheumatic disease, it is most frequently seen in association with SJIA. Viral infections, such as EBV, are common triggers. Early diagnosis can often be challenging due to the lack of validated diagnostic criteria and overlapping features with sepsis-like syndromes or flares of the underlying rheumatic disease. Generally, MAS should be considered in all rheumatic patients who present with persistent fevers, a drop in ESR and platelet count, especially in the setting of coagulopathy and rising ferritin levels.

PUZZLING PROTRACTED PAROXYSMS OF HYPOXIA

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A 75-year-old never-smoking man with a thirty-year history of unexplained episodes of hypoxia presents with a profound recurrence. He reports no environmental exposures, familial lung disease, recent pneumonias, or history of immunosuppression. He was well until he experienced a presumed atrial fibrillation associated stroke three months prior to admission. He subsequently underwent an unsuccessful cardiac ablation, after which he was noted to have worsening hypoxia, requiring 15-L of high flow oxygen. Evaluation was notable for a positional component suggestive of platypnea and orthodeoxia. Diagnostic studies yielded essentially normal pulmonary function tests, a negative CT pulmonary angiogram, and a bubble transthoracic echo (TTE) with a questionable intra-atrial shunt, which was followed by a normal right heart catheterization. He was transferred to our institution for ongoing assessment of his refractory hypoxia. On arrival his 15-L oxygen requirement reappeared upon sitting for lung auscultation, confirming his enigmatic clinical syndrome as compatible with platypnea-orthodeoxia syndrome (POS).

The POS is associated with numerous diseases, but is generally attributed to three separate causes: intracardiac shunt, pulmonary AV shunt, and V/Q mismatch. Many clinicians associate POS with hepatopulmonary syndrome but the literature increasingly recognizes the major contribution of intracardiac shunting. Typically one associates right-to-left interatrial shunting with chronic or intermittent increases in right sided pressures. However, intracardiac shunting in POS occurs in the setting of normal right-sided pressures. For this to occur, the POS requires contributions of both anatomic and functional components. Anatomic conditions are typically intra-atrial defects such as patent foramen ovals (PFO), atrial septal defects, or fenestrated atrial septal aneurysms. The most prevalent functional influence is a body position change such as sitting or standing from supine, resulting in an architectural distortion whereby normal venous return is shunted through the defect directly to the left atrium.

In our patient, a repeat bubble TTE, (then confirmatory TEE), demonstrated a “wind sock” PFO with right-to-left atrial jet providing the likely anatomical cause of this patient’s symptoms. He was taken to the catheter lab for endovascular PFO closure and was confirmed to have normal right-sided heart pressures. He symptomatically improved almost immediately following the procedure, and was discharged two days later, off oxygen, doing well. A follow-up office visit two months later demonstrates continued symptomatic relief without complication or need for supplemental oxygen.

This man’s story offers the opportunity to review the pathophysiology of POS as well as highlight an uncommon, but likely underrecognized syndrome. The most common associated anatomic anomaly in POS is PFO. Highlighted by the thirty-years of functional impairment in our patient, and the availability of potentially curative treatment, clinicians need to be vigilant as early testing and intervention may lead to reduced testing and improved quality of life for our patients.

AN ATYPICAL AND UNRECOGNIZED PRESENTATION OF HYPERHOMOCYSTEINEMIA

First Author: Jayson R. Baman Second Author: Justin R. Baman

Hyperhomocysteinemia is a known risk factor for cardiovascular disease, commonly presenting as cerebrovascular accidents in teenagers and young adults.

A 27-year-old man with a history of bipolar disorder presented to the Emergency Department with complaints consistent with pleuritic chest pain. The patient endorsed mild dyspnea and troponin measurement was slightly elevated. Soon after presentation, the patient's symptoms subsided and he was subsequently diagnosed clinically with myopericarditis. Thus, although an EKG was ordered by the attending physician in the Emergency Department, the patient's EKG results were not interpreted.

Five months later, the patient presented again with chest pain that was this time sharper and exacerbated by deep inspiration. He denied syncope, dizziness and paroxysmal nocturnal dyspnea. Emergency cardiac catheterization revealed complete occlusion of the right coronary artery, as well as complete occlusion of the proximal to mid-portions of the left anterior descending artery. EKG was consistent with an old anterior myocardial infarction—likely from his episode several months earlier—and echocardiogram revealed akinetic segments of left ventricular wall near the anterior apex and septum. A thrombus was documented in the left ventricle chamber, and physical exam was negative for carotid and abdominal bruits. Significant coronary collateral vessels articulated with the left anterior descending artery, suggesting that this occlusion was likely the result of chronic thrombus formation. The patient was treated with balloon dilatation and stenting.

Given the patient's age, hypercoagulability was a suspected mechanism for these episodes of acute coronary syndrome. Labs revealed significantly elevated homocysteine with all other relevant bloodwork within normal limits. The patient was diagnosed with hyperhomocysteinemia. The patient denies family history of early-age coronary disease or stroke, recurrent abortions and hypercoagulability.

This case describes an unusual presentation of a well-documented etiology of hypercoagulability in young adults. By retrospective analysis, the patient's original presentation in the Emergency Department was consistent with an anterior myocardial infarction. Because his symptoms subsided relatively quickly, the attending emergency physician neglected to pursue full work-up for hypercoagulability. This patient's case reveals the importance of a complete cardiovascular workup in a young patient with signs of acute coronary syndrome. He was fortunate to survive two complete coronary occlusions. Earlier detection and identification of the patient's hyperhomocysteinemia would have allowed for appropriate intervention to reduce the prospective risk of coronary events.

CYTOTOXIC EDEMA...THE SEQUELAE OF SYNTHETIC MARIJUANA "SPICE"

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A 22 year old male patient was admitted to the ICU after being found unresponsive with possible drug overdose from K2 and heroin. He had no significant PMH except well controlled asthma. Upon arrival to ED, patient appeared agitated and was not alert or oriented. His vitals were Temp: 102.8 rectally; HR: 128; BP: 194/116; RR:32; O2Sat: 94 on non-rebreather mask. Patient was intubated for airway protection. Urine tox was positive for opioid. Physical examination showed a reactive 3mm dilated right pupil and 2mm dilated left pupil as well as decreased breath sounds at bases. Patient moved all extremities in agitation but did not open eyes or follow commands and was determined to be GCS 3. CT head was negative. As we did not have history upon patient arrival and because he was febrile and altered, LP was performed and was negative. Chest XR showed b/l perihilar infiltrates. CT of chest/abd/pelvis showed diffuse airspace consolidation, most notably in the lower lobes and the basilar regions of the upper lobes most consistent with aspiration pneumonitis. Concerned about possible anoxic brain injury, an MRI brain was ordered. Interestingly, MRI brain revealed diffusion restriction, consistent with cytotoxic edema involving the cerebellum, the posterior parietal cortices and the right caudate nucleus head, most marked in the cerebellum. Further workup with an EEG showed moderate encephalopathy consistent with toxin induced injury. Despite aggressive pulmonary therapy and supportive measures, over the next few days, patient's neurologic status continued to decline. Physical exam showed 5mm dilated and fixed right pupil, 3mm dilated and fixed left pupil, corneal reflex present on right, negative on left, absent gag/cough reflex and unchanged GCS 3 since admission. Repeat MRI showed new onset supratentorial hydrocephalus with dilated lateral and third ventricles with mild increase in cytotoxic edema in the frontal cortices and in the left lateral parietal cortex. Unfortunately, within the next few days, patient was declared brain dead and support was withdrawn.

Synthetic cannabinoids are gaining popularity among recreational drugs because of their reputation for attaining the same euphoria while still being legal. Marketed as "K2" or "Spice", these drugs of abuse are known to be associated with serious side effects such as tachycardia, rhabdomyolysis, seizures, acute psychosis, cardiac ischemia and ischemic stroke. However, the dangerous sequela of cytotoxic edema secondary to synthetic cannabinoid use has not yet been documented. With the rising demand for these attractive drugs, healthcare providers should be made aware of this new and devastating side effect which our case highlights.

ARM YOURSELF WITH KNOWLEDGE: A SKIN CANCER THAT CAUSES PARALYSIS

Erin Lowe, BA, Timothy Brown, MD, and William A. Geary, MD, PhD

INTRODUCTION: Perineural invasion (PNI) is seen in 5% of cutaneous Squamous Cell Carcinomas (cSCC). The trigeminal and facial nerves are most commonly involved, and few cases of cSCC with PNI outside of the head and neck are reported.

CASE: A 91 year old male presented to his surgeon in 2015 for evaluation of two elevated lesions of the left arm, present and growing for one year. History is significant for a cSCC of the left posterior wrist, excised in 2012. He also has progressive left arm weakness since 2013 with episodes of twitching of the arm, head and neck. He was evaluated by a neurologist. CT and MRI of the brain were unremarkable. EEG suggested seizure activity. Nerve conduction studies showed significant involvement of radial, median, and ulnar nerves. During surgical excision there was gross invasion of skeletal muscle, vessels, and nerves. Histology yielded SCC with multifocal PNI. Comparison of slides with the prior original cSCC of the left wrist yielded histologic similarities.

DISCUSSION: It is possible that the initial cSCC on the wrist invaded the radial nerve with neurotropic propagation retrograde throughout communicating branches, creating distal motor deficits. Neurological, surgical and histological findings support this pattern of spread. Due to the aggressive nature of PNI it is recommended to treat with Mohs resection to clear nerve margins and postoperative salvage radiotherapy. The patient refused further surgery and will be undergoing radiotherapy consisting of 6000 cGy in 30 fractions delivered over six weeks in an attempt to cease further perineural spread.

UVEITIS, APHTHOUS ULCERS, AND ARTHRALGIAS: A MISSED OPPORTUNITY FOR EARLY DIAGNOSIS

Caitlyn Moss, Britt Marshall, Simon Mucha

CASE PRESENTATION: We present the case of a 58 year old woman with recurrent uveitis, painful oral and esophageal ulcers, wrist pain, abdominal cramping, and fatigue. She had an extensive workup by multiple physicians over the past 2 years including an EGD showing esophageal ulcers, CT abdomen suggestive of mild colitis, elevated erythrocyte sedimentation rate (65 mm/hr), and negative titers for anti-saccharomyces cerevisiae antibodies (ASCA), rheumatoid factor, ANA, and anti-CCP.

She then presented to our emergency department with bloody diarrhea, diffuse arthralgias, chills, perirectal lesions, 12 kg weight loss, and erythematous, ulcerated macules on her hands and knees. CT abdomen showed colonic wall thickening and pericolonic fat stranding. Colonoscopy showed eroded, granular, inflamed, and ulcerated mucosa and a stricture at the splenic flexure. Pathology showed active chronic colitis, ulcers, and non-caseating granulomas, confirming the suspected diagnosis of Crohn's disease.

DISCUSSION: Crohn's disease (CD) is an inflammatory bowel disease characterized by non-continuous transmural lesions anywhere along the gastrointestinal tract. Classic symptoms include abdominal pain, diarrhea, bloody stools, fatigue, and perianal disease.

Our patient highlights some of the extra-intestinal manifestations, which include aphthous ulcers, uveitis, arthropathies, and neutrophilic dermatoses, which may precede gastrointestinal symptoms. Other manifestations are primary sclerosing cholangitis, erythema nodosum, and pyoderma gangrenosum.

ASCA titers are not sensitive enough to rule out CD. The gold standard for diagnosis is colonoscopy, which should be pursued in any patient where CD is suspected to allow earlier diagnosis and appropriate treatment of Crohn's to prevent complications such as strictures in our patient.

PAINFUL LIMB, DUSKY TOES, INTACT PULSES: A CASE OF VENOUS LIMB GANGRENE

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Gangrene of the digits or skin is typically associated with arterial occlusions. However, gangrene and skin necrosis may occur with intact arterial pulses due to thrombotic pathogenesis within the venous circulation; this clinical entity – venous limb gangrene – is not well recognized and can have major consequences if not promptly treated.

A 24-year old woman presented to the hospital with pain and swelling of her right lower extremity (RLE), a rash on her right thigh and cyanotic right toes. Three weeks prior to admission the patient was diagnosed with an unprovoked deep vein thrombosis (DVT) of her RLE and pulmonary emboli, treated with enoxaparin, and then bridged to warfarin. Ten days prior to admission, she returned to the ED with worsening bilateral lower extremity pain and swelling, was found to have worsening of her RLE DVT and a new left lower extremity DVT. Her International Normalized Ratio (INR) was subtherapeutic at 1.7. Due to extensive clot burden, she underwent catheter-directed thrombolysis of the RLE DVT and received perioperative heparin. She was bridged to warfarin and discharged. One day later she returned to the hospital with excruciating RLE pain. Her exam revealed a new 4 x 5 cm irregular, erythematous lesion on the right anterior thigh, and her right foot toes were cyanotic. Bilateral dorsalis pedis pulses were located via Doppler. Laboratory studies revealed an INR of 6.8, prothrombin time of 89 sec (normal: 10.3 – 13.5 sec), PTT of 55.6 sec (normal: 26.7 – 36.2 sec), platelet count of 121 K/mm³ (two weeks earlier: 466 K/mm³), plasma D-Dimer of 67,196 ng/mL (normal: <230 ng/mL), Factor VII of 0.01 U/mL (normal: 0.50 – 1.50 U/mL), and protein C of 0.23 U/mL (normal: 0.78 – 1.32 U/mL). She was administered vitamin K and fresh frozen plasma, and started on argatroban for suspected heparin-induced thrombocytopenia (HIT). She was admitted to the Burn Unit and received pain control with hydromorphone. The HIT antibody test was strongly positive. Within two days, the cyanosis of her toes resolved; however, her right anterior thigh lesion continued to evolve, becoming multiple large hemorrhagic bullae. She underwent anterior thigh skin debridement with an autologous skin graft. Pathology from the thigh revealed fibrinoid thrombi in the dermal and subcutaneous venules, and the patient was diagnosed with venous limb gangrene associated with warfarin in the context of HIT.

This case demonstrates venous limb gangrene, a rare clinical entity associated with warfarin-induced imbalance between procoagulant and anticoagulant mechanisms in the context of heparin-induced thrombocytopenia. Prompt recognition and treatment, including cessation and reversal of warfarin, as well as systemic anticoagulation with a non-heparin agent, can save both life and limb.

AN ANTERIOR MEDIASTINAL MASS: A RARE INCIDENTAL FINDING ON LUNG CANCER SCREENING

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Introduction As the U.S. Preventive Services Task Force 2013 (USPSTF) lung cancer screening guidelines continue to be applied, more primary care internists will be faced with complex decisions in regards to follow-up and referrals of incidental findings. In this case we report an incidental mediastinal mass that after aggressive and high-risk work-up was successfully diagnosed and treated. We discuss the rarity of the case, and the implications and need of further guidance for the primary care internist in an increasingly common scenario.

Case Description A 65-year-old man with a 3 year history of fatigue presented to the internal medicine clinic to establish care with a new primary care provider. He had a 60 pack-year smoking history and following the 2013 USPSTF lung cancer screening guidelines recommendations, low-dose chest CT (LDCT) was ordered. Results demonstrated an incidental anterior mediastinal mass measuring 2.8cm by 1.8cm adjacent to the right side of the heart. Patient was referred to vascular surgery and PET-CT showed a similarly-sized hypermetabolic mass with standardized uptake value (SUV) of 3.3. Robot assisted mediastinal exploration with resection was attempted, but was incomplete due to patient instability. The retrieved specimen confirmed a well-differentiated thymic carcinoma (type B3 thymoma) measuring 6.5cm by 4.5cm by 2cm with microscopic invasion through the thymic capsule into the parathymic fat, with no associated lymphovascular space invasion noted, thus meeting Masaoka Stage IIA criteria. Post-operative radiation therapy for the residual disease was performed with sustained remission to date.

Discussion Incidental findings on LDCT are common, with some studies reporting that up to 65.2% of patients have at least 1 incidental abnormality. Although the majority of these abnormalities are eventually deemed to be clinically insignificant (e.g. atelectasis), up to 26.9% of patients had findings requiring further workup, which in most studies define “clinically significant findings.” Authors have noted that the distinction between “clinically significant” and “clinically insignificant” incidental findings widely varies. Given the widespread use of the 2013 USPSTF lung cancer screening guidelines, the primary care provider, ultimately, will be increasingly forced to make this distinction and to timely and adequately refer or reassure patients based on a complex differential diagnosis. In this case, we report an incidental thymic carcinoma, a rare and deadly cancer if left untreated. The Early Lung Cancer Action Project (ELCAP) screening study revealed that 71 out of 9263 individuals (0.77%) had an incidentally discovered mediastinal mass, and of these masses, only 3 cases (0.03%) of newly diagnosed cancer were detected (1 thymic carcinoma and 2 esophageal cancers). The patient described in the case was part of the 0.03% of the screening population who benefits from an aggressive, costly, and high-risk diagnostic work-up and treatment. Do we expect our primary care internists to continue to make these decisions without clear decision-making guidance?

SCIMITAR SYNDROME PRESENTING AS PULMONARY HYPERTENSION IN AN 87 YEAR OLD FEMALE.

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Scimitar syndrome, a variant of partial anomalous pulmonary venous connection is a rare congenital cardiovascular disorder that occurs in 0.5-0.7 % of the general population. It is characterized by terminal insertion of the right pulmonary vein into the inferior vena cava and is associated with right lung hypoplasia, dextraposition of the heart, and anomalous systemic collaterals from the aorta to the right lung. The literature describes two main forms based on age of presentation: (1) The infantile form, when patients <1 year old present with pulmonary hypertension, hemoptysis, tachypnea, or heart failure; these cases often require surgical intervention and have a poor prognosis. (2) The adult form, where the diagnosis is often made incidentally during imaging studies, patients are usually asymptomatic or present with recurrent pulmonary infections and exertional dyspnea; they rarely require intervention. Shunt volume likely plays a role in determining which form develops.

We present a case of an 87 year old female with scimitar syndrome presenting with symptoms associated with the infantile form. She is, to our knowledge, the oldest patient described in the literature with this syndrome. She had a history of paroxysmal atrial fibrillation and flutter, stroke and hypertension, when she presented with worsening shortness of breath on minimal exertion. An echocardiogram was performed that showed dextrocardia, RVSP 120-125 mmHg, normal LV, severe RVE, moderate LAE, severe RAE, moderate aortic stenosis, moderate aortic regurgitation, and severe tricuspid regurgitation. These results were worsened compared to an echo the year prior: RVSP 46, normal RV, normal LV, dilated LA, normal RA, and normal IVC. CT angiogram showed a large single pulmonary vein draining all the blood from the right lung in to the IVC just above the diaphragm (partial anomalous pulmonary venous return), congenital hypoplasia of the right lung, and dextrocardia. Further hemodynamic evaluation including heart catheterization was recommended but our patient chose conservative management and was started on sildenafil. Despite early improvement in exercise capacity along with decreased RVSP, she later continued to deteriorate and died with hypoxia and right heart failure.

This patient had a significant left to right shunt resulting in overcirculation of the pulmonary vasculature, increased shear stress and ultimately increased pulmonary vascular resistance with pulmonary hypertension and right heart failure. Thus her condition most closely resembles WHO group 1 pulmonary arterial hypertension associated with congenital heart disease. What is most unusual in her case is that her pulmonary hypertension presented at such an advanced age. PAH has been described in younger adults, and the infantile and adult form of PAPVC represent extremes on a continuum of disease presentation. We have presented a rare case of scimitar syndrome in an elderly female with transient improvement of her pulmonary hypertension on empiric phosphodiesterase-5 inhibitors.

DOUBLE TROUBLE AT THE WATERPARK

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Pneumonia remains a leading cause of hospitalizations worldwide, with a 20%–30% mortality rate. The differential for possible infective etiologies is quite broad and environment-specific considerations can significantly help narrow down the most likely suspect. Nonetheless, as reported here, polymicrobial etiologies should be considered.

A 57-year-old woman presented with a five day history of dysarthria, fevers and chills. Five days ago, she returned from a trip to a waterpark in San Antonio when she developed fevers, chills, and a frontal headache. The following day, she developed slurred speech, shortness of breath, nausea, vomiting and loose watery diarrhea. On presentation, she had a temperature of 39.8 degrees Celsius, heart rate of 127 beats per minute, blood pressure of 97/58 mmHg, and respiratory rate of 29 with an oxygen saturation of 92% on room air. Computed Tomography (CT) of her chest showed a right upper lobe infiltrate and right pleural effusion. Magnetic resonance imaging (MRI) of her brain revealed restricted diffusion in the splenium of the corpus callosum and central pons, with mild corresponding FLAIR hyper-intensity. She had a serum sodium of 127 mmol/L, blood urea nitrogen of 41mg/dL and creatinine of 1.7 mg/dL. Her blood contained 11,000 white blood cells/ μ L with 94% neutrophils. She was given 5 liters of fluid and started on Moxifloxacin, Piperacillin-Tazobactam, and Vancomycin. On the third day of hospitalization, the Legionella urine antigen test resulted positive. Her sputum gram stain, blood cultures, and acid fast bacilli smear did not show any organisms. Her symptoms resolved and she was discharged on fourteen days of Moxifloxacin. Approximately seven weeks later, her Acid fast bacilli (AFB) culture started to grow *Mycobacterium fortuitum* complex, an organism identified by matrix assisted laser desorption/ionization time-of-flight spectrometry (MALDI-TOF). She was alerted about the findings and returned to the hospital with symptoms of shortness of breath, night sweats, chills, and fatigue. X-ray of her chest showed resolution of the right upper lobe infiltrate and a dominant calcified granuloma in the right hilum while head MRI revealed resolution of the lesion in the splenium of the corpus callosum and central pons. She was started on therapy with Moxifloxacin and Clarithromycin.

In environments involving water systems such as water parks and cooling towers, *Legionella pneumophila* takes precedence due to its strong association with respiratory infections in these settings. However, the same water systems are suitable milieus for potentially pathogenic non-tuberculous mycobacteria such as *Mycobacterium fortuitum*. As reported here, both etiologies may present concurrently in the setting of exposure to water systems. Accordingly, in assessing the etiology of a respiratory infections associated with exposure to water systems, internists should avoid anchoring biases associated with *Legionella*, and instead expand their differential to include non-tuberculous mycobacterial species.

WHERE'S WALDEN? A CASE OF WALDENSTROM MACROGLOBULINEMIA DISGUISED AS MULTIPLE MYELOMA

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Introduction: Overall incidence of Waldenstrom Macroglobulinemia, WM, is about 3 per million persons per year. In the United States, 1500 new cases are diagnosed each year. IgM monoclonal gammopathy can be seen in both multiple myeloma and WM. It is important to distinguish between these two diagnoses because treatment options vary and can have severe implications.

Case report: An 80-year-old woman presented with weakness and rigors and was hospitalized for a UTI with bacteremia treated with antibiotics. Prior to her hospitalization, her primary care physician was concerned about a lab showing hyperproteinemia. Hematology-Oncology was consulted to evaluate patient for multiple myeloma. Patient denied skeletal events and her only complaint was fatigue, which was thought to be due to her 10-day hospitalization. Labs were ordered including CBC, CMP, SPEP, and a free light chain assay. Labs returned showing a normocytic anemia, thrombocytopenia, worsening renal function (Creatinine 1.19, GFR 44), hyperproteinemia (Protein 9.6), and hypoalbuminemia (Albumin 2.9). Serum electrophoresis showed a thick monoclonal protein band consistent with a monoclonal gammopathy. However, serum immunofixation revealed a biclonal gammopathy with an elevated IgG (4086) and IgM (1291). Kappa/ Lambda free light chain ratio was elevated at 6.47. These results were strongly suggestive of multiple myeloma and plans were made for treatment with lenalidomide. A bone marrow biopsy was ordered, which showed hypercellular marrow with a diffuse kappa restricted lymphoplasmacytic B-lymphoid infiltrate. Moreover, G-DNA FISH panel showed normal signal pattern for all probes on multiple myeloma panel.

Discussion: Results were consistent with a mature B-cell lymphoproliferative disorder with plasmacytic differentiation. Multiple myeloma was ruled out and lenalidomide therapy was canceled. Patient's main complaint of fatigue and the results from her thorough workup eventually led to a diagnosis of WM and treatment with rituximab. Most lymphoplasmacytic lymphomas are Waldenstrom Macroglobulinemia with an IgM monoclonal gammopathy, and less than five percent are IgA or IgG gammopathies. However, this case illustrates a unique presentation of WM in which a biclonal gammopathy of IgG and IgM was discovered. The presence of biclonal gammopathy makes classification of this lymphoproliferative lymphoma challenging. In addition, the plan to start lenalidomide for what appeared to be multiple myeloma would not have been first line treatment for this disguised diagnosis of WM. Moreover, it could have potentially worsened her anemia. This case illustrates the importance of completing a thorough investigation in order to obtain an accurate diagnosis and more importantly, to provide the best treatment for the patient.

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POST R-CHOP CHEMOTHERAPY INDUCED SYSTEMIC SCLEROSIS IN A PATIENT WITH DIFFUSE LARGE B-CELL LYMPHOMA

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Learning objectives:

1. Systemic sclerosis can develop after chemotherapy with Daunorubicin and Cyclophosphamide in patients with diffuse large B cell lymphoma.
2. Understand mechanisms by which systemic sclerosis can follow lymphoma therapy.

Case: Our patient is a 48-year-old African American lady, with a history of stage III diffuse large cell lymphoma. Her only PMH was sickle cell trait. She underwent R-CHOP chemotherapy, subsequently entering remission. Four months after completion of chemotherapy she started having shortness of breath and also noted thickening of the skin of her hands. Symptoms gradually progressed over the next decade to involve orthopnea, PND and distal fingertips turning blue in cold temperatures. She slowly also developed esophageal dysmotility. Due to her progressive breathlessness she presented to our hospital. On exam BP 132/103, HR 91, RR 24. Cardiac: regular, no rubs, gallops, or murmurs. Decreased breath sounds and bilateral crackles in basilar lungs. She could not flex her wrists and fingers due to taut and thick skin consistent with sclerodactyly. Calcinosis cutis was present.

ANA, ANCA and anti centromere B antibodies were negative. Anti scleroderma-70 antibody was positive at high titers. CT chest showed honeycombing and fibrosis in lung bases. ECHO showed mildly enlarged left atrium, left ventricle and right atrium, low ejection fraction of 25%. Heart catheterization showed normal coronaries, consistent with non-ischemic scleroderma cardiomyopathy.

Given the onset of symptoms first starting after 4 months of completion of chemotherapy, insidious worsening over the next decade, positive antibody for SCL-70, progressive lung fibrosis, non-ischemic cardiomyopathy, sclerodactyly, calcinosis, Raynaud and esophageal dysmotility, a diagnosis of chemotherapy-induced systemic sclerosis was made.

Discussion: Certain chemotherapeutic agents have been linked to systemic sclerosis. Bleomycin, Docetaxel, and Paclitaxel have been implicated. However, very few cases regarding systemic sclerosis following treatment with Cyclophosphamide and Daunorubicin (present in R-CHOP) have been reported. Four such reports highlight systemic sclerosis developing between 7 months to 8 years after finishing chemotherapy.

Another common link between lymphoma and systemic sclerosis is Epstein Barr virus (EBV). EBV is a well known causal agent in the development of B cell lymphoma. EBV also targets fibroblasts, which are the principal mediators of fibrogenesis in systemic sclerosis. Studies document the presence of EBV non coding small RNAs (EBERs) in fibroblasts and endothelial cells in the skin of systemic sclerosis patients.

Systemic sclerosis may also be a consequence of a robust host anti-tumor immune response, which kills lymphoma tumor cells. The auto antibody specifically associated with such a response is against RNA polymerase III.

CULPRIT IN CAMO: KSHV-ASSOCIATED MULTICENTRIC CASTLEMAN'S DISEASE

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Introduction Most life threatening opportunistic infections in HIV patients occur when their CD4 counts drop below 200 cells/mm³. However, Kaposi's sarcoma herpes virus (KSHV)-associated multicentric Castleman's disease (MCD), a rare lymphoproliferative disorder, tends to strike HIV patients with relatively intact CD4 counts. Moreover, patients typically present with nonspecific symptoms, including fever, generalized lymphadenopathy, weakness, and night sweats. These disease characteristics make KSHV-associated MCD a formidable diagnostic challenge.

Case Presentation A 49-year-old man diagnosed with HIV two years earlier and started on antiretroviral therapy two months prior presented to a clinic with fever, diffuse palpable lymphadenopathy, and shortness of breath. His CD4 count and viral load were 480 and 127,000, respectively. He was admitted to the hospital and treated for MRSA pneumonia. Shortly after treatment was initiated, he developed a diffuse, maculopapular rash consistent with a drug eruption, which improved when his medications were changed. During the hospital stay, the patient also underwent a cervical lymph node biopsy with instructions to follow-up on an outpatient basis to receive the results. The patient was discharged home.

Five days later, the patient was readmitted after presenting with a worsening pruritic, papular rash and progressive, diffuse edema including angioedema of his upper lip. He also had continued lymphadenopathy as well as new violaceous skin lesions on his chest and feet. CT scan of the chest showed interlobular septal and peribronchovascular thickening, pleural effusions, mediastinal and axillary adenopathy, and splenomegaly. Laboratory testing showed normocytic anemia, thrombocytopenia, and leukocytosis. CD4 count was 544, and viral load was 19,000. Biopsy of the new skin lesions revealed Kaposi's sarcoma. The results of the lymph node biopsy from the previous stay revealed a plasma cell variant KSHV-associated MCD.

He received rituximab and was later placed on cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy. The patient's symptoms improved over the next two weeks, and he was then discharged home with an appointment for additional CHOP therapy.

Prior to the next scheduled appointment, the patient presented to the ER with progressive dyspnea. He coded in the ER and never recovered. Sputum cultures were positive for MRSA. He was placed on comfort care and passed away several days later.

Discussion This case illustrates the potential to identify MCD early in the course of the disease, particularly where an HIV patient presents with nonspecific symptoms including fever and diffuse lymphadenopathy. Clinicians should have MCD high on the differential whenever an HIV patient with a relatively normal CD4 count presents with nonspecific symptoms such as those described above. Recognition of this disease early in its development is critical to prevent or slow progression of disease.

FISHING FOR THE SOURCE: A RARE GI INFECTION

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Intro: *Raoultella planticola* is a Gram-negative bacterium phylogenetically similar to *Klebsiella* species, and has been a relatively harmless cause of human infection in the past. However, reports of severe infections and drug-resistant strains have increased in recent years.

Case Report: A 69-year-old male with a history of chronic constipation secondary to colonic redundancy, Barrett's esophagus, and cirrhosis presented to the ER with severe diarrhea, hypotension and fever to 38.2°C. Despite fluid resuscitation, patient remained in shock and was admitted to the intensive care unit for vasopressor support. Vancomycin and piperacillin/tazobactam were started on admission.

Physical examination was notable for abdominal distension and left lower quadrant tenderness. Stool studies for *Shigella*, *Salmonella*, *Campylobacter* and *Clostridium difficile* were negative, but admission blood cultures were positive for Gram-negative bacilli, later speciated as *Raoultella planticola* pan-susceptible to typical antibiotics except ampicillin. The patient continued having large output of foul smelling diarrhea. Serial abdominal radiographs revealed progressive colonic dilatation, and abdominal computerized tomography showed extensive sigmoid colon dilatation reaching 12.7 cm, as well as colonic mucosal thickening consistent with infectious colitis. Laboratory tests revealed leukocytosis of 13,200/mm³, anemia and hypokalemia, which, along with radiographic and clinical findings, met criteria for diagnosis of toxic megacolon. The patient was treated with piperacillin/tazobactam with significant improvement of diarrhea and downgraded from the intensive care unit, but distention later recurred. Gastroenterology was consulted for colonoscopy with decompression. No obstruction was seen, and repeat blood cultures were negative. Eventually, the patient tolerated parenteral nutrition and recovered from infection.

On further questioning, the patient recalled eating leftover fish brought over by a neighbor the day his symptoms started, and could recall no other sick contacts prior to hospitalization. Also of note was a history of numerous recent endoscopic procedures.

Discussion: At least 20 cases of *Raoultella planticola* have been reported since 1984, with most in the last 2 years. Cases are most often associated with neoplasia, or recent trauma or invasive procedures (e.g. endoscopy). Other common risk factors include: male gender, Caucasian race, age over 50, and presence of gastrointestinal comorbidities. *R. planticola* in humans seems to have an affinity for intra-abdominal colonization, but has also presented as respiratory, urinary, and skin and soft tissue infections. A few cases report infection after ingesting fish or seafood, and cases involving carbapenem-resistant strains have also been documented.

Important bacterial causes of toxic megacolon include *Clostridium difficile*, *Campylobacter*, *Entamoeba*, *Salmonella* and *Shigella spp.* The mainstays of treatment are antibiotics, fluid resuscitation, and colonic decompression. To our knowledge, we present the first documented case of toxic megacolon from *R. planticola* associated with fish ingestion. *Raoultella planticola* should be considered an emerging pathogen capable of severe gastrointestinal infections in high risk patients, and providers should be watchful for antibiotic resistance.

CRANIOPHARYNGEAL MYASTHENIA MASQUERADING AS CRANIAL POLYNEUROPATHIC GUILLAIN BARRE SYNDROME.

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Introduction: Guillain Barre syndrome (GBS) involving multiple cranial nerves is a rare mimic of isolated craniopharyngeal myasthenia gravis.

Case: An 83-year-old male presented with a feeling of thickness of the tongue and perioral paresthesia of 2-days duration. He was sent home with high dose prednisone for angioedema. He presented in 2 days unable to close either eye, exhibiting bilateral facial weakness, and choking on his pills and food. His circumoral paresthesia persisted. He also was “off balance”. He reported a mild upper respiratory infection a few days prior. He denied similar illness in the past and his family denied having noticed any fluctuating weaknesses or eye droop in the past. Exam revealed irregular and sluggishly reacting pupils (surgical left pupil from old trabeculectomy), markedly diminished eye blink, complete inability to close his eyes, symmetric facial flattening and inability to puff his cheeks. His palate and uvula were symmetrically immobile. He had absent gag reflex and choked on swallow testing. Tongue movements were quite restricted and his speech had prominent hypernasal tone. Except mildly impaired joint position sensation, his sensory exam was normal. He had asymmetrically diminished deep tendon reflexes (absent ankles, triceps) but motor strength in the limbs and torso was normal. He was very ataxic on his feet, although his finger nose testing failed to reveal coordination issues. The symmetric craniopharyngeal involvement, facial sensory symptoms, diminished reflexes, and ataxia roused suspicion of cranial nerves polyneuropathy variant of GBS. However myasthenia gravis was also suspected. He was intubated soon due to respiratory failure and started on a 5-day-course of intravenous immunoglobulin (IVIG) infusion. In the next 10 days, he recovered his craniopharyngeal strength and was extubated. His swallowing still showed impaired relaxation of lower esophagus, requiring tube feeds. He was discharged to rehabilitation.

His nerve conduction study of the face failed to show any evidence of demyelination or axonal insult, however repetitive stimulation showed decrement. His blood tests for Acetylcholine receptor binding, modulating and blocking antibodies came back unequivocally elevated. Ganglioside antibodies for GBS and Miller Fisher variant were negative. These suggested the diagnosis of myasthenia gravis.

Discussion: The presence of facial sensory symptoms, weakness of eye closure rather than lid droop, ataxia and the absence of similar illness in the past are clinical features unusual for myasthenia. Electrophysiological studies and antibody testing may be required to clinch the definitive diagnosis in many cases, although acute phase treatment is the same, ie., IVIG or plasmapheresis.

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY: DEBILITATING AND DEADLY

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With improved highly active anti-retroviral therapy (HAART) for treatment of human immunodeficiency virus (HIV), there has been substantial reduction in acquired immunodeficiency syndrome (AIDS)-related opportunistic infections. Despite medical advances, some infected individuals develop opportunistic infections, including a devastating neurological disease: progressive multifocal leukoencephalopathy (PML).

We present the case of a 55 year-old HIV infected, treatment-naïve, African-American female with a CD4 count of 7 (1.6%) and viral load of 170,000 copies, presenting with new onset headache described as “being hit with a sledgehammer,” vertigo, gait instability, left sided facial numbness, left sided blurred vision, exertional dyspnea, nausea, and a 30 pound unintentional weight loss over 3 months. Physical exam was significant for decreased sensation in the left V1-V3 distribution, intention tremor, tandem gait ataxia, negative Romberg, normal heel to toe walk, and normal heel to shin. Head computed tomography demonstrated poorly defined left cerebellar hypodensity. Magnetic resonance imaging, T1 weighted, revealed non-enhancing T2 signal increase involving cerebellar white matter, with mass effect upon the fourth ventricle; supratentorially, there were multiple smaller foci of white matter enhancement. JC Virus (JCV) DNA was detected in her cerebrospinal fluid. Detection of JCV with her presentation supported diagnosis of PML. Mirtazapine was started for poor appetite. The patient clinically improved and HAART was initiated in the outpatient setting. The patient deteriorated in follow-up and was found to have discontinued mirtazapine. She was diagnosed with immune reconstitution inflammatory syndrome (IRIS) and started on high-dose steroids. Additionally, mirtazapine was resumed due to its potential neuroprotective role in PML.

PML is characterized by multifocal neuronal demyelination and histopathology demonstrates oligodendrocytes with enlarged nuclei and viral inclusions. Typical presentations include visual field defects, cognitive impairment, weakness, and ataxia. PML is found most often in AIDS patients, but can be found in patients with other immunosuppressive conditions, including malignancy, chronic inflammatory disease, or recent transplants. Dozens of reports describe PML in patients undergoing treatment with natalizumab, efalizumab, and rituximab. Prognosis is poor; there are no effective treatments and 1 year survival is 50%. Additionally, up to 80% of surviving patients have neurological sequelae. Reversing immunosuppression provides the best opportunity for disease stabilization. Patients with a CD4+ count over 300 and a non-detectable viral load have the best prognosis. However, initiating HAART can cause IRIS, leading to worsening disease. Patients receiving immunomodulatory antibodies may have therapy suspended and plasma exchange performed to remove circulating antibodies. Case reports describe mirtazapine and mefloquine as potential agents to halt disease progression, but neither has been investigated in clinical trials. Mirtazapine downregulates 5HT_{2a} receptors used by the JCV to enter glial cells and preliminary research suggests mirtazapine decreases intracellular viral replication in vitro. Further research is needed to establish clinical benefit.

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HIDDEN IN PLAIN SIGHT: DIAGNOSING AN AUTOIMMUNE BLISTERING DISEASE

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Autoimmune blistering diseases are rarely encountered on inpatient internal medicine services and have a wide differential.

A 50 year-old Caucasian male presents with complaints of not eating for the past two weeks secondary to odynophagia. The patient was well until two months before presentation when he noticed rapid onset of oral ulcers, unilateral eye erythema, and diffuse blisters. The patient was treated as an outpatient with sulfamethoxazole/trimethoprim, with no improvement. The patient was subsequently given a two-week treatment of Prednisone, with reported resolution of the patient's symptoms. This was followed by a two week taper, which resulted in a resurgence of the skin lesions. The patient denied any sick contacts, genital lesions, joint pain, or recent viral illness. Physical exam was significant for extensive mucosal ulceration, scalp excoriations, sclera-conjunctivitis, and diffuse ruptured bullae with occasional eschar formation on the patient's forehead, back and thigh. The patient had a positive Nikolsky's sign. The patient's CBC and chemistries were within normal limits, except for an anion gap metabolic acidosis that resolved with fluids. The patient labs were negative for HIV, Hepatitis B, Hepatitis C, ANCA, ANA, and RF.

The etiology was presumed to be autoimmune with the differential diagnosis including Behçet's disease and Pemphigus vulgaris. Behçet's disease, a systemic vasculitis, was favored by significant oral ulceration and skin findings. The patient did not have significant genital lesions or arthritis. Furthermore, the patient had conjunctivitis instead of the traditional uveitis seen in Behçet's disease. The patient's blisters in different stages of healing and positive Nikolsky's sign favored Pemphigus, which generally does not have ocular involvement. Given the diagnostic uncertainty, skin biopsy was performed to differentiate the neutrophilic vascular infiltrate more consistent with Behçet's versus an epidermal blisters with positive immunofluorescence for desmoglein-3 more consistent with Pemphigus vulgaris. The patient's biopsy was consistent with Pemphigus vulgaris and the patient improved with systemic corticosteroids, except for worsening eye erythema. The patient was sent to ophthalmology who subsequently diagnosed the patient with HSV keratitis.

This case demonstrates an uncommon presentation to an internal medicine service as well as a differential diagnosis for autoimmune blistering diseases requiring skin biopsy for certain diagnosis. Furthermore, it demonstrates the dangers of combining seemingly related symptoms into a syndrome, while they could be due to different etiologies.

COIL EMBOLIZATION IN TREATMENT OF SCIATICA

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Disk rupture and degenerative spine disease are the most common causes of sciatica. There are however, less common non-spinal causes.

A 79-year-old retired male carpenter with a history significant for numerous high falls and electrocution presented as a new patient with left sided lower back pain radiating into the hip, anterior thigh, and toes. Both back and left leg pain was described as 7/10, intermittent, and located posterior to the left greater trochanter. During exacerbations, he could not stand, ambulate, or sleep at night. He denied numbness or weakness, as well as any precipitating traumatic events. The patient had seen physiatry, interventional pain medicine physicians, a chiropractor, had two corticosteroid injections, and was taking pregabalin, tramadol, and prednisone. None of these interventions helped with the pain. Physical examination revealed a robust gentleman in no acute distress. No sensorimotor deficit was noted distal to reported sites of pain. Deep tendon reflexes were normal and symmetric. Gait was antalgic, and hip/leg pain was elicited with straight leg raise to angle between 30 and 70 degrees on the left. An MRI of the left hip without contrast done the month prior showed a gluteal venous varix compressing the sciatic nerve from the sciatic notch distally for a length of 10 cm.

The patient was diagnosed with sciatica due to direct compression of the left sciatic nerve by a gluteal varix. After several consultations, the patient underwent an ultrasound- guided transcatheter coil embolization of the left internal obturator and superior gluteal varices. Seven months later, the patient stated that his pain had much improved, was minimal and intermittent, and that he was able to walk at least a mile without problems.

This case illustrates two points. First, gluteal varices can cause sciatica by impingement on the sciatic nerve, and thus, should be considered in the differential for treatment-resistant or atypical sciatica presentations. Second, it is possible to successfully treat such cases using a less invasive endovascular approach, instead of the more commonly reported surgical ligation/ resection of varices.

ILIOFEMORAL VENOUS COMPRESSION PRESENTING AS INAPPROPRIATE SINUS TACHYCARDIA

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More than 20% of patients with chronic venous insufficiency (CVI) have obstruction of the iliofemoral or ilio caval veins.¹ However, iliofemoral venous obstruction remains one of the most underdiagnosed conditions worldwide, as the clinical manifestations are diverse and poorly understood. External compression resulting in iliofemoral obstruction due to May Thurner Syndrome, pregnancy, bladder distension, common iliac artery aneurysms, endometriosis and malignancy, has been associated with independent adverse cardiac outcomes.²⁻⁶

A 40 year old female presented to her primary care physician with recurrent episodes of palpitations, near syncope and fatigue for more than five years, exacerbated by minimal activity. She reported chronic fatigue, lower back pain radiating to the posterior thighs and bilateral leg swelling. She denied prior cardiac history. Holter monitoring revealed heart rates in the 120s-130s, and 150s with minimal activity. CMP, CBC and thyroid function tests were normal. Physical examination was consistent with overweight habitus, ankle edema, hyperpigmentation, cold lower extremities and pre-ulceration, with high CEAP and VCSS scores. Echocardiogram revealed an EF > 65% and no valvular heart disease. A diagnosis of inappropriate sinus tachycardia (IST) was made.

Vascular evaluation with venous ultrasound and mapping revealed loss of phasic waves and significant blunting of the waveforms in the bilateral common femoral veins (L>R), and deep vein reflux in the femoral veins, suggesting unexplained high grade iliofemoral compression or May Thurner Syndrome. Venography with intravascular ultrasound (IVUS) evaluation revealed subtotal occlusion of the left common iliac vein with a compressed mean luminal area (MLA) of 75 mm². IVUS guided stenting resulted in a MLA of 212 mm². Clinical symptoms started improving within three days post-procedure. Repeat holter monitoring at 6 weeks demonstrated resting heart rates in the 80s and exercise heart rates of 110-120. Patient resumed her activities of daily living without limitations and reported resolution of her leg pain, swelling and back pain at 3 month follow up.

This case demonstrates that iliofemoral venous obstruction may result in significant preload reduction, resulting in IST as a compensatory response to maintain cardiac output. Patients with signs or symptoms of CVI and associated tachyarrhythmias should be evaluated for iliofemoral venous obstruction, as it may significantly impact preload status and correlate with negative cardiac outcomes. Further large scale studies can prove to be valuable in understanding the association between iliofemoral venous obstruction and its effects on cardiac function.

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NYSTAGMUS OF CORTICAL ORIGIN: A CASE OF REFLEX SEIZURES

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INTRODUCTION: Nystagmus is an involuntary rhythmic oscillatory vertical or horizontal jerking of the eyes. While vestibular pathology and strokes of the brainstem or cerebellum are most often considered in patients presenting with significant nystagmus, rare cortical lesions can result in nystagmus as well.

CASE DESCRIPTION: A 58-year-old female presented with a brief and transient spell of aphasia, seizure-like activity, and residual left hemiparesis. Upon admission the patient began experiencing multiple spells of unique semiology: her eyes would gaze leftward, her head would turn leftward, then a slow saccade of both eyes to the left and a fast "corrective" jerky movement of both eyes to the right would ensue. This was accompanied by an extensor "fencer" posturing of the left forearm. These spells, which were inducible with leftward gaze, lasted 10-30 seconds. She remained alert and oriented and able to speak through them, and could be redirected to look to the right to abate the eye jerking.

Her exam was otherwise normal. She smoked 1 pack per day and took statin for hyperlipidemia. Electroencephalogram (EEG) showed focal slowing over the lesion. Brain MRI revealed a 3.2cm lesion in the posterior-superior right frontal lobe with surrounding edema. Angiography showed a largely thrombosed arteriovenous malformation (AVM) supplied by the right middle cerebral artery, surrounded by venous congestion explaining the restricted diffusion in MRI. Functional MRI brain with finger, toe taps and verb generation paradigms demonstrated that the lesion spares the primary motor strip but partly involves the premotor areas. The patient elected not to undergo surgery at this time; her spells responded to antiepileptic therapy with levetiracetam, and edema around the lesion subsided with concomitant steroid therapy.

DISCUSSION: This patient's spells were characteristic of a hyperactivation of the supplementary motor cortices and a diagnosis of 'reflex focal seizures' was made. Normally, the frontal eye fields (FEF) of the premotor cortex push the eyes contralaterally in an effort to correct and maintain conjugate gaze. Irritated by the AVM, the right FEF in our patient pushed the eyes to the left (slow phase), and a corrective action from the left FEF caused fast phase of the nystagmus to the right. While evaluating a patient with new-onset nystagmus, it is important to remember this cortical mechanism and investigate beyond the traditional vestibular, brainstem, and cerebellar sources of pathology.

NOT ALL PNEUMONIA IS PNEUMONIA

Syed Ali Shawn Naqvi

Idiopathic interstitial pneumonia is best described as a non-infectious process that can masquerade as a common pulmonary infection. The hallmark of idiopathic interstitial pneumonia is interstitial inflammation of the lungs most often caused by inflammatory conditions or medications resulting in excess granulation tissue in the bronchioles and surrounding lung tissue. The inflammatory response can mimic that of infectious etiology such as fever, cough, and dyspnea, making it difficult to distinguish from commonly seen community or hospital acquired pneumonias.

A 54 year old male presented to the emergency room with increasing lip swelling, shortness of breath, fevers, cough and fatigue. A clinical diagnosis of angioedema secondary to losartan was made. The losartan was held and the patient was started on H1/H2 blockers and steroids. Within the course of the hospitalization lab work indicated leukocytosis of 22.4 and a chest xray showed bilateral nodular opacities consistent with an underlying infectious process in the context of the patient's symptomatology. Given the patient's clinical condition and history he was started on empiric therapy for community acquired pneumonia with ceftriaxone and azithromycin. Following two days of treatment the patient's clinical condition improved resulting in discharge with outpatient completion of antibiotic course and cessation of antihistamine/steroid therapy. Two days following discharge the patient returned to the hospital with worsening dyspnea, cough and fatigue. The patient's overall condition dramatically deteriorated symptomatically with continual fevers at 38.2 and leukocytosis of 23.4. The decision was made to empirically start antibiotics to cover healthcare associated pneumonia with vancomycin and cefepime as well as pan-culturing with specific testing for HIV and alternative pathogens such as tuberculosis, histoplasmosis and sporothrix. HIV testing along with all alternative pathogen analysis noted above produced unremarkable results. Without improvement in the patient's clinical condition a bronchoalveolar lavage was performed which also showed unremarkable findings on cytology. Over the next two days the patient's condition gradually improved with reduction of leukocytosis to 13.2 and cessation of cough and fever. The decision was made to follow up outpatient for biopsy to determine precise etiology of disease. The pulmonary consultants made the preliminary determination of idiopathic interstitial pneumonia in spontaneous remission based on the patient's clinical findings, history, demographics and response to treatment with biopsy result pending to determine the exact subset of idiopathic interstitial pneumonia.

This case demonstrates the importance of exploring non-infectious causes for a pneumonia-like syndrome. Although less commonly seen, the realm of interstitial idiopathic pneumonias is significant and broad enough to warrant closer investigation. The focal teaching point emphasizes the necessity of clinicians to not only explore rare and non-rare causes of infection in possible pneumonia but to diversify into other disciplines such as non-infection as in the case of idiopathic interstitial pneumonia.

SOMETIMES WHEN YOU HEAR HOOVES, IT IS ZEBRAS: TUMOR LYSIS SYNDROME AS THE CAUSE OF NEW ONSET SEIZURES IN A PATIENT WITH SOLID ORGAN CANCER WITH MULTIPLE BRAIN METASTASES

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Introduction: Tumor lysis syndrome (TLS) is an oncologic emergency characterized by constellation of metabolic derangements (hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia) caused by the rapid breakdown of malignant cells. The metabolic derangements cause the clinical manifestations characteristic of the syndrome, including acute kidney injury, seizures, cardiac dysrhythmias, and sudden death. TLS most commonly occurs within days of initiation of cytotoxic chemotherapy in liquid malignancies. TLS is extraordinarily rare in solid malignancies - a review of the literature shows that there have only been 131 total reported cases of TLS in patients with solid tumors and only 5 in patients with bronchogenic adenocarcinoma [1, 2].

Case Description: A 51 y/o male with h/o widely metastatic bronchogenic adenocarcinoma presented with new onset seizures. He was being treated with chemotherapy, changed to ceritinib a month ago, and was on daily dexamethasone. He was also receiving palliative whole-brain and lumbar-sacral spinal radiotherapy for metastases found on recent MRIs.

In the ED, his seizures were thought to be secondary to his brain metastases. Further down the ED differential were intracranial hemorrhage and electrolyte abnormalities. CT head was negative. Initial labs showed – AKI (creatinine 5.7 mg/dL from a baseline of 1.0 mg/dL), hyperkalemia (7.1 mmol/L), and hypocalcemia (6.4 mg/dL). EKG was normal sinus rhythm. Patient was treated with keppra for seizure prophylaxis and his hyperkalemia was medically managed.

In the ICU, in light of patient's widely metastatic malignancy, significant AKI, hyperkalemia, and hypocalcemia, workup for tumor lysis syndrome was conducted. The workup showed hyperuricemia (15.4 mg/dL) and hyperphosphatemia (6.2 mg/dL). With these laboratory findings, patient met laboratory and clinical criteria for TLS. He was treated with rasburicase (urate oxidase), electrolyte repletion, and fluids. Chemo and radio therapy were held. The patient had no further seizures. Over the course of several days his electrolyte abnormalities and AKI resolved.

Discussion: This case illustrates that while extraordinarily rare TLS can still occur in solid malignancies and shows the potential dangers of having a narrow differential diagnosis. TLS should always be on the differential in any cancer patient presenting with new onset AKI, seizures, and/or dysrhythmias, as a delay in diagnosis can be life-threatening at worst and cause significant morbidity at best in an already ill patient population.

TLS is very simple to rule out via laboratory studies, but is easy to miss in patients who have an alternative, more common explanation for their symptoms, such as in this case where the patient's seizures were thought to be secondary to his brain metastases. This case demonstrates that developing a thorough differential is one of the most important parts of taking care of patients. With more time it would have been clear to the initial providers that brain metastases were an unlikely cause of the patient's presentation, as the metastases were very small and the patient was on daily dexamethasone, and that TLS should be ruled out.

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A CASE OF METHAMPHETAMINE-INDUCED ALVEOLAR HEMORRHAGE

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Introduction: Methamphetamine is well known for its effects on neurotransmitters in the brain, resulting in behavior changes such as impulsivity, delusions, and psychosis. However, pulmonary disease resulting from methamphetamine is uncommon.

Case: A 42 year-old woman with a history of methamphetamine abuse had been on a three week methamphetamine “binge,” both snorting and ingesting methamphetamine. She presented to the emergency department with three days of progressive hemoptysis and headache. Her chest x-ray showed bilateral infiltrates and chest CT demonstrated diffuse patchy ground glass opacities. She was started on broad-spectrum antibiotics. Bronchoscopy was performed with a progressively bloodier return obtained during bronchoalveolar lavage, indicating alveolar hemorrhage. She developed worsening hypoxia and pulmonary infiltrates requiring high flow supplemental oxygen. Bronchoscopic cultures were negative. Coagulation studies were normal as were tests for HIV, ANA, ANCA, and anti-glomerular basement membrane antigen. Complement studies revealed a decreased C4 and normal C3. BAL cell count and differential revealed a marked neutrophilic alveolitis. She was started on high dose intravenous corticosteroids for a presumptive pulmonary vasculitis with prompt clinical improvement. She was discharged on hospital day nine without the need for supplemental oxygen, and her hemoptysis resolved one week after discharge. Prednisone was tapered and stopped one month after discharge. At three month follow up she was asymptomatic. Chest x-ray and oxygenation were normal and she remained abstinent from methamphetamine.

Discussion: We believe this presentation represents a case of alveolar hemorrhage secondary to methamphetamine use. We considered other causes of acute respiratory failure with diffuse infiltrates such as congestive heart failure and infection. However, bronchoscopic cultures were negative and there was no evidence of fluid overload on exam. We initially suspected an underlying connective tissue disease, but clinical evaluation by a rheumatologist was not supportive of this diagnosis, and serologies were negative.

Published literature supports our hypothesis that methamphetamine causes a pulmonary vasculitis. Cocaine, another central nervous system stimulant, is known to cause pulmonary hemorrhage when inhaled. In addition, several case reports describe a central nervous system vasculitis associated with methamphetamine use that was responsive to corticosteroid treatment. Indeed, our patient’s neutrophilic alveolitis and rapid response to corticosteroids is consistent with an immunologically mediated process such as a small vessel vasculitis.

In **conclusion**, alveolar hemorrhage should be suspected in methamphetamine users presenting with hemoptysis or pulmonary infiltrates. The use of high dose corticosteroids should be considered in these patients if evaluation for infectious causes is unrevealing.

ACUTE RIGIDITY, FEVER AND HIGH-DOSE ANTIPSYCHOTICS: A LESSON IN PATIENT SAFETY

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Case: A 52-year-old woman presented to the hospital with left leg pain after a fall. She had a history of heavy alcohol use, cirrhosis, non-ischemic cardiomyopathy, and delirium during a recent hospitalization. Admission x-ray showed a left tibial plateau fracture and she underwent operative repair. The patient developed prolonged post-operative confusion. For two weeks, she was treated with scheduled quetiapine and as needed intravenous haloperidol, one 1 mg dose daily.

Three weeks post-operation, she became acutely agitated and was treated with intramuscular haloperidol. She received five 2 mg doses over three days. On the third evening, she had a temperature of 37.7C and a heart rate of 118 bpm. Exam showed diaphoresis and mild upper extremity rigidity. Laboratory studies included creatinine 0.79 mg/dL, creatine kinase 1431 units/L, and WBC 10,810 per mm³. Haloperidol was stopped due to concern for neuroleptic malignant syndrome (NMS).

Four hours later, her temperature was 40.3 C. Exam showed diffuse rigidity and agitation. She was treated with intravenous lorazepam. The patient had received her home dose of sertraline since admission, and this medication was stopped. Serum creatinine rose to 0.97 mg/dL but returned to baseline, and creatine kinase peaked at 4931 units/L. The patient received decreasing doses of lorazepam for one week. She was calm and oriented to person and place on discharge to a skilled nursing facility. The patient passed away four weeks later due to intestinal ischemia.

Discussion: NMS is a challenging diagnosis. It is associated with a classic triad of fever, muscle rigidity and altered mental status, which was present in this case. However, providers must distinguish NMS from other drug-induced syndromes such as serotonin syndrome (SS). In this case, laboratory tests helped differentiate the two syndromes: elevated serum lactate dehydrogenase, creatine kinase, and WBC count suggested NMS. Timing is also important: NMS usually presents several days after drug administration while SS usually presents in less than twelve hours.

This case is also a relevant patient safety event. NMS is a known, rare complication of antipsychotic medications such as haloperidol. While the exact pathophysiology of NMS is not known, rapid dose escalation of antipsychotics is a risk factor. Several system factors led to rapid dose escalation in this case. First, multiple transitions in care occurred. Four physicians were involved in this patient's care 24 hours prior to the adverse drug reaction. A fifth physician had placed the original medication order two days before the event. Additionally, the medication was ordered on an "as needed" basis. Therefore, nursing staff was not required to communicate each use with a physician or pharmacist. Another important aspect was the patient's underlying hepatic dysfunction. Electronic order entry systems do not routinely cross-check new medication orders with diagnoses that affect drug metabolism. Rare adverse medication reactions such as this one are opportunities to improve medication safety.

PYELONEPHRITIS IN THE ABSENCE OF PYURIA

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Introduction: Acute pyelonephritis (APN) is usually diagnosed clinically with pyuria or other evidence of infection on urinalysis such as positive leukocyte esterase or positive nitrites in combination with fever, costovertebral angle tenderness, dysuria and increased urinary frequency. In the absence of these indicators diagnosis can be delayed.

Case: An 18-year-old female with no significant past medical history presented with a home temperature of 105, upper right quadrant abdominal pain and headaches. She denied diarrhea, nausea, vomiting, dysuria or increased urinary frequency, cough, congestion, recent illnesses, or rashes/lesions. She met SIRS criteria with a recorded fever of 105.3 and tachycardia to 127 without a clear source for sepsis.

RUQ ultrasound was not indicative of cholecystitis, pregnancy test was negative, and UA was negative for nitrites, leukocyte esterase, WBCs, and bacteria. She was found to have 2+ blood in her urine but it was thought to be secondary to active menstruation. CT abdomen/pelvis showed ureteral wall thickening concerning for APN vs possible small infarcts but with unremarkable UA it was felt that APN was unlikely. Further work up indicated starvation ketosis and anion gap metabolic acidosis and she was resuscitated with 5% IV dextrose. She decompensated quickly requiring ICU care and continuous fluid resuscitation for unstable hypotension. With an unknown source for her overwhelming infection further diagnostic labs were sent and she was started empirically on IV meropenem with little improvement. Coverage was then broadened to IV meropenem, IV vancomycin, and a single dose of IV gentamycin. Further diagnostic tests included blood and urine cultures for aerobic, anaerobic, fungal and mycobacterial, and serology for west nile virus, California encephalitis, HIV, EBV, CMV as well as rheumatic work up including ANA, ANCA, ESR and CRP. All were negative with the exception of the urine culture which was positive for 60,000 CFU/ml *Enterococcus faecalis* sensitive to ampicillin, ciprofloxacin, nitrofurantoin, and vancomycin. She remained on IV vancomycin until her vitals improved and then was de escalated to PO Amoxicillin for a total treatment time of 10 days. Pt was completely asymptomatic 4 weeks later and is pending a CT abdomen/pelvis to ensure complete resolution of infectious process.

Discussion: APN is a frequent condition encountered by hospitalists and requires a high index of suspicion for clinical diagnosis, as prompt antibiotic therapy is critical to prevent sepsis and subsequent hemodynamic compromise. While it is widely accepted that APN can present with the absence of positive cultures, nitrites or leukocyte esterase on UA it is less frequent to consider pyelonephritis in the absence of pyuria. It is important for hospitalists to recognize that APN can occur in the absence of urine leukocytes to prevent clinical worsening due to delayed diagnosis and antibiotic therapy.

METFORMIN-INDUCED LACTIC ACIDOSIS: A SHOCK-ING SIDE EFFECT

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Lactic acidosis is a rare but potentially fatal side effect of metformin. Known risk factors include heavy alcohol use and impaired liver and renal function.

A 55-year-old man with a PMH of DM II on metformin “felt wrong” during a night of drinking. Family presumed he was drunk and laid him to bed. Next morning, family couldn’t arouse him and called EMS, who found him screaming about back pain. En route to the hospital, the patient became more hypotensive and unresponsive with a glucose of 30. He arrived to the ED with temperature 89.2, blood pressure 75/37, pulse 47, and respiration 30. He was intubated and eventually received maximal drips of four vasopressors only to maintain MAPs in the 50s. Labs showed creatinine 3.73, WBC 17.3, TSH 20.87, lactic acid level 26, and alcohol level 0.056. ABG showed pH 6.66, PCO2 23, and bicarb 2.4. UDS, and salicylate and Tylenol levels were unremarkable.

The differential for this patient’s shock included cardiogenic, hypovolemic, and septic etiologies. Cardiogenic shock was thought to be unlikely due to negative troponins and hyperkinetic wall motion on echo. Hypovolemic shock, potentially secondary to hemorrhage, was unlikely due to patient’s normal hemoglobin throughout the admission. The patient was initially put on broad spectrum antibiotics. However, septic workup including urinalysis, blood cultures, CXR, and CTs of the chest, abdomen, and pelvis came back negative for any definitive source of infection.

Prognosis was poor on the night of admission and a long family discussion led to the patient becoming DNR. However, through supportive ICU care, the patient stabilized, improved, and underwent further testing. Cortisol and ACTH tests were negative for adrenal failure. Renal ultrasound, abdominal X-ray, and abdominal CT were also noncontributory.

The patient continued to improve through his hospital course. By discharge, most of his lab markers had normalized. He still had residual dysphasia, cognitive communication deficits secondary to hypoxic encephalopathy, and kidney failure and anuria with creatinine up to 7.2 requiring hemodialysis. However, he had good affect, was motivated to improve, and was able to stand with balance, ambulate with a walker, and have bed mobility with minimal assistance. He was eventually discharged with follow-up and home PT.

This case illustrates a severe and potentially fatal adverse reaction to metformin in someone with previously normal kidney and liver function. Due to its rarity, early recognition of shock symptoms in patients on metformin is critical to instituting timely multisystem supportive care to reduce mortality. Additionally, a case is made for ordering a metformin level in the evaluation of patients who present with shock of undetermined etiology.

THE GREAT PRETENDER: MORE THAN MEETS THE EYE

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Introduction: Syphilis has emerged in the last decade as a formidable infectious disease in the United States, with the rates of primary and secondary syphilis doubling since the turn of the century. Ocular manifestations of syphilis present less commonly, though the true epidemiology is unclear. We present a rare case of ocular syphilis presenting as unilateral blurriness.

Case: A 29-year old previously healthy bisexual African-American male presented with a three-week history of right eye blurriness. Ophthalmology was consulted and performed a dilated fundus exam that revealed a right eye with severe vitritis, panuveitis and retinal vasculitis and a left eye with mild vitritis. Snellen vision of R 20/300 and L 20/30 was noted. Extensive workup to evaluate for Lyme disease, sarcoidosis, tuberculosis, syphilis, toxoplasmosis, and rheumatic disease was performed.

Workup revealed a positive serum treponemal antibody testing (FTA-Abs) and RPR (1:256). Patient was admitted for treatment with aqueous crystalline penicillin-G 3 million units every 4 hours for a 14-day duration. A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis revealed lymphocytic pleocytosis (97%), leukocytosis (22), and elevated protein (54), all highly characteristic findings of neurosyphilis. CSF VDRL studies were negative, however. Upon examination, patient had multiple genital chancres along the base of his glans penis. Skin examination revealed tan-brown macules and patches along the right palm and the plantar surfaces of his feet bilaterally. Neurological exam was unremarkable, other than the noted visual deficits. Subsequent workup for HIV was positive with a CD4 count of 255. With treatment, patient reported gradual improvement in right eye vision and improvement in vitreous haze on ophthalmic exam. He was referred to a local HIV/AIDS clinic for continued therapy.

Discussion: Ocular syphilis, an insidious but potentially sight-threatening illness, has been of special concern for the CDC which has seen an alarming rise in the number of cases over the past two years. The rising rates of primary and secondary syphilis may be largely attributed to unprotected sex in a time period of major advances in HIV treatment.

The CDC has issued a clinical advisory regarding the increasing incidence of ocular syphilis, especially in the men who have sex with men population. The condition most commonly presents as posterior uveitis or panuveitis, two conditions with many infectious, autoimmune, and rheumatic mimickers. Of note, CSF VDRL may be falsely negative in up to 70% of patients as in the case presented. Clinicians should have a high index of suspicion for a syphilitic etiology in patients presenting with the characteristic ocular complaints and a suggestive social history.

Sponsored Meals and Honoraria and Physician Prescribing Patterns

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Background: In 2009, 84% of American physicians reported receiving meals, gifts, or payments from the pharmaceutical industry. Although industry-sponsored meals and honoraria may create opportunities for physicians to discuss new therapies, past studies using self-reported data have raised concerns about their potential to influence prescribing behavior. We used recently released data from the U.S. Sunshine Act to conduct the first national, physician-level analysis of the association between industry-sponsored meals and honoraria and physician prescribing patterns.

Methods: In this retrospective cohort study, we linked U.S. Sunshine Act data with prescribing data from Medicare Part D. We identified physicians who wrote prescriptions in any of four drug classes: selective serotonin and serotonin-norepinephrine reuptake inhibitors (SSRIs and SNRIs), β -blockers, angiotensin-converting-enzyme inhibitors and angiotensin-receptor blockers (ACEis and ARBs), and statins. We identified the most-prescribed branded drug in each class (desvenlafaxine, nebivolol, olmesartan, and rosuvastatin, respectively), and used Sunshine Act data to flag physicians who received meals or payments for that drug from August-December 2013. Multivariate logistic regression was used to compare prescribing rates of each drug relative to alternatives, among physicians who received meals or payments and physicians who did not. Sensitivity analyses were conducted using propensity-score matching. We excluded research-related and royalty payments, and adjusted for physician-level demographic characteristics, specialty, and practice setting.

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- **Results:** 279,669 sample physicians received 63,524 payments associated with the four drugs, totaling \$1.4 million. Sponsored meals constituted 95% of target payments, and averaged under \$20. Physicians receiving one sponsored meal for the drug of interest had significantly higher rates of prescribing desvenlafaxine over other SSRIs or SNRIs (odds ratio 2.18, 95% confidence interval 2.13 to 2.23), nebivolol over other β -blockers (1.70, 95% CI 1.69 to 1.72), olmesartan over other ACEis or ARBs (1.52, 95% CI 1.51 to 1.53), and rosuvastatin over other statins (1.18, 95% CI 1.17 to 1.18). The association was dose-dependent, with additional meals and costlier meals associated with greater increases in relative prescribing rates ($p < 0.001$). Results were similarly significant in propensity-matched cohorts. Physicians receiving honoraria, which averaged \$1,065, were significantly more likely to prescribe the targeted drug over alternatives (odds ratios of 1.20 to 2.03 across the four drugs studied, $p < 0.001$)
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- **Conclusions:** Sponsored meals or honoraria from a drug's manufacturer are associated with increased prescribing of that drug relative to alternatives. Further investigation of physician-industry relationships is needed to determine their potential impact—positive or negative—on healthcare costs and patient outcomes.

INCIDENCE OF VENOUS THROMBOEMBOLISM (VTE) IN PATIENTS PRESCRIBED MEGESTROL FOR APPETITE STIMULATION

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Introduction: Cachexia and anorexia occur in 50-80% of cancer patients. In cancer patients, it is associated with shorter survival, treatment failure, early treatment termination, declining functional status, and reduced quality of life. Megestrol acetate is a synthetic derivative of progesterone commonly used to treat cancer-related cachexia. Megestrol use is associated with thromboembolism among other adverse events. VTE has been reported to occur in 4.9% to 32% of patients on megestrol therapy. This is of particular concern since the risk of VTE in patients with cancer is already increased several-fold. The primary endpoint is to determine whether a higher incidence of VTE exists in cancer patients prescribed megestrol for appetite stimulation when compared to cancer patients not prescribed the drug.

Methods: This is a retrospective study conducted via chart review with two groups: study (patients prescribed megestrol) and control (patients not prescribed megestrol) at a National Cancer Institute (NCI) designated cancer center. The sample size was 435 patients (study group n=217; control group n=218) attaining a power of 90%. Patients who were prescribed megestrol were identified using the inpatient pharmacy department charge codes. Sex, high risk disease, active chemotherapy, advanced cancer stage, advanced age, poor performance status (ECOG greater than or equal to 3), major surgery, prior history of VTE, and high dose dexamethasone use were the variables examined. Exclusion criteria included patients less than 18 years old, those outside of the time frame of the study (1.5 years), and those without cancer diagnosis. Chi-square test, non-parametric Wilcoxon, and a multi-variable logistic regression model were used.

Results: Uni-variable analysis showed that advanced cancer stage, active chemotherapy, active cancer, and poor performance status were statistically significant (p value < 0.0001). After adjusting for these, patients in the study group were noted to have a higher incidence of VTE with odds ratio of 3.1 (95% CI 1.3-7.7) with p value <0.0001. Sex, advanced age, high risk disease, prior VTE history, major surgery, and high dose dexamethasone use were not statistically significant. Patients with advanced cancer stage had a higher incidence of VTE when prescribed megestrol compared to control (odds ratio 3.4; 95% CI 0.975-12.09).

Conclusions: Patients with cancer prescribed megestrol for appetite stimulation have a higher incidence of VTE, especially patients with advanced cancer stage. Development of VTE in this population can further worsen quality of life and create unnecessary burden with anticoagulation treatment and its complications. The initiation of alternative appetite stimulants that do not further increase the risk of VTE in cancer patients should be considered. To our knowledge, this study is the largest to date to analyze the incidence of VTE in cancer patients prescribed megestrol and can impact the way practitioners treat cachexia/anorexia in cancer patients.

A Novel Compound, Membrane-Tethered E2, Selectively Activates the ER Rapid Signaling Pathway – Implications for Vascular Benefit

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Introduction: Heart disease is the leading cause of death in both men and women in the United States despite disproportionately affecting men. In younger post-menopausal women, estrogen supplementation may decrease the risk of heart disease through its interaction with ER α and ER β in the vasculature. Upon binding ER, estrogen initiates two pathways: the rapid signaling pathway and the genomic signaling pathway, traditionally associated with dilatation of vessels and proliferation of endothelial cells, respectively. Estrogen supplementation, however, has been associated with an increased risk of breast and uterine cancer. Here we hypothesize that isolating the rapid pathway alone, using the novel compound membrane-tethered E2 (MT E2), is sufficient to mediate the beneficial vascular effects of estrogen without inducing the potential adverse effects.

Methods: Human endothelial somatic hybrid cells (EA.hy926) were treated with 100 nM MT E2 with the appropriate ligand controls. Activation of the rapid signaling pathway was measured by phosphorylation of specific downstream proteins (eNOS, AKT, and ERK). Activation of the genomic signaling pathway was measured by an ERE-luciferase assay. ER α was localized by immunocytochemistry, and proliferation and migration were measured by a cell viability and scratch-wound assay, respectively.

Results: Cells treated with MT E2 exhibited increased phosphorylation of eNOS, AKT, and ERK, suggesting that MT E2 activates the rapid signaling pathway. Cells treated with MT E2 did not, however, upregulate luciferase via an estrogen response element (ERE), suggesting that MT E2 is incapable of activating the genomic pathway. Unlike treatment with E2, MT E2 did not drive ER α to the nucleus, though it did induce proliferation and migration of vascular cells to an equal or greater extent than E2, suggesting that the rapid pathway is sufficient to induce vascular cell function.

Conclusions: In conclusion, we confirmed our hypothesis that the novel compound, MT E2, activates the ER rapid pathway without activating the genomic pathway, and by doing so, is sufficient to induce proliferation and migration of human endothelial cells to an equal or greater extent than conventional estrogen, supporting its potential vascular benefit in vivo.

EpxDiabetes accelerates blood glucose control for patients with diabetes

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Introduction: Blood glucose control for diabetics remains a difficult goal to achieve among patients, in particular because of inconsistent communication of blood glucose values to physicians outside of office visits. Blood glucose diaries have low compliance rates, and underlying socioeconomic issues, medication side effects, and medication non-compliance contribute to blood glucose control difficulties. To address these issues, we designed, implemented, and piloted an inexpensive automated text message (SMS) and phone communication system, EpxDiabetes, to aid in the management of Diabetes.

Methods: EpxDiabetes was designed based on interviews with academic and community physicians and patients at Washington University in St. Louis, Mercy Hospital, and the Family Care Health Center. EpxDiabetes sends regular prompts to patients to report their fasting blood glucose (FBG) via SMS or phone call. The system algorithmically adapts to the patient's needs and can vary message frequency appropriately. If the patient reports a FBG value beyond set thresholds, their provider receives an actionable alert. For longitudinal monitoring, EpxDiabetes provides a regular report prioritized by average FBG levels. In this pilot, a total of 35 patients were followed for over 8 weeks at Mercy Hospital and Washington University in St. Louis while tracking response rates and average FBG levels.

Results: Preliminary results show that, on average, 86% of patients respond to the system each week. We have found that patients using EpxDiabetes for 8 weeks have experienced a 34.6 point reduction in FBG from a baseline calculated as the average of the first week of reported FBG values. In these patients, median baseline was 168.1 with an interquartile range of 158.8 to 196.5. In addition, we have been able to identify and alert providers in real-time to 11 cases of acute hypoglycemic or hyperglycemic events over the 8-week period for the 35 patients initially recruited. We also report a cost-benefit analysis that demonstrates the capability of EpxDiabetes to be sustainable and generate revenue for practices via novel fee-for-service codes.

Discussion: EpxDiabetes is a novel system that leverages an inexpensive, widely adopted technology to provide clinically relevant information to the provider and efficiently improve patient-provider communication. In an initial pilot, EpxDiabetes demonstrated strong patient engagement and retention as well as beneficial effects on FBG levels in diabetes patients. A 400-subject randomized controlled trial to assess the impact of this system on HbA1c reduction and patient compliance will begin in January 2016, with interim findings available by May 2016.

A community-based approach to cardiovascular risk reduction in northern New Mexico

First Author: Ingrid Lindquist Joshua Brown MD Christopher Bunn DO

Introduction and background: Hypertension is the most common modifiable risk factor of premature cardiovascular disease and events. One in three American adults have hypertension and about half of those with a formal diagnosis do not have it controlled. A major challenge in reducing the prevalence of hypertension is that it is a chronic, progressive and asymptomatic condition. While hypertension is a serious medical condition, there are well-defined and effective ways to monitor and control it with medical and lifestyle interventions. Therefore, improving early detection efforts and access to and use of medical care has the potential to considerably reduce the rate of hypertension and its consequences.

According to state cause-of-death records, New Mexicans under the age of 75 have increased mortality due to hypertension relative to national rates, most notably in Hispanic and Native American men. We hypothesize that limited access to primary care is a significant factor leading to this and other health disparities in the state.

Current estimates of hypertension and cardiovascular disease burden in northern New Mexico are limited to data collected from national surveys like the Behavioral Risk Factor Surveillance System, hospital records and state death records. These epidemiological estimates have been found to underestimate disease burden in communities, particularly those with significant minority populations. Thus, improved community-specific disease burden assessments are necessary to accurately determine risk and can profoundly impact the resources allocated to at-risk communities.

Community blood pressure screening has been utilized as a public health strategy for decades. Recent studies on this method of intervention found that public screening coupled with direct medical referral is most effective in improving blood pressure control. In order to facilitate a reduction in cardiovascular risk, a clear route to medical follow-up is vital.

We present our efforts in a community blood pressure screening, education and medical referral program called Impact Heart Health (IHH), a collaborative quality improvement (QI) community health project with the non-profit Impact Health New Mexico in Santa Fe, NM.

Methods and Results: To date we have screened 380 individuals for high blood pressure at 28 community events primarily in Santa Fe, providing individuals with heart health education and medical referral. In addition to direct services to community members, we evaluate the rates of hypertension in the community as well as risk factors of smoking history and access to primary care. Up-to-date results will be presented at the ACP conference.

Conclusions: We present the structure of our ongoing community program as a successful model of community engagement and community-based participatory research in northern New Mexico that includes disease screening, health education, medical referral and assessment of risk factor burden.

STUDENT RESEARCH POSTER FINALISTS

Work-Life Balance of Women Physicians

First Author: Jamie Bering MS Lacey Pflibsen BS Priya Radhakrishnan MD

Introduction: As the number of practicing female physicians continues to rise each year, female attitudes regarding careers in medicine have become a rising topic of interest. In 2010, approximately 30.4% of active physicians in the United States were female while 46.1% of the residents and fellows that year were female. Given the traditional role of women in the family unit and professional workplace, we want to assess if and what types of personal life decisions women physicians postpone in pursuit of career success. We hope to help evaluate and describe specific factors that can affect the social context of the medical culture driven by female physicians as well as potentially expose any associations that may exist.

Methods: An electronic survey was created and distributed via an email link to the survey website, Survey Monkey. Over 500 surveys were distributed to female physician faculty and staff of local area health systems as well through various women's physician organizations. Responses were maintained as anonymous. Eight surveys were eliminated for incompleteness leaving 110 surveys included in this preliminary analysis. The primary endpoint was whether or not a personal decision had been deferred in pursuit of a medical career. Secondary endpoints assessed whether there was any correlation with other variables including age, relationship status, number of children, and specialty type.

Results: Preliminary data shows that personal decision deferments were endorsed by 62.73% of respondents. Of these, 76.81% reported waiting to have children and 39.13% reported waiting to get married. The majority of the women who reported deferments were aged 41-50 years (46.38%) while the majority of women who denied deferments fell in the 31-40 age range (34.15%) closely followed by women in the 41-50 year age range (29.27%). The relationship status of respondents was comparable between groups. Pediatric specialties accounted for 31.7% of the women in the non-deferment group, while the career types in the deferment group were more variable. Of note, however, is that the deferment group included more physicians in internal medicine and surgical specialties compared with the non-deferment group. Women in the non-deferment group had an average 2.24 children, while those in the deferment group had an average of 1.87 children. Finally, while 97.56% of women in the non-deferment group would choose medicine again as a career, only 77.14% of women in the deferment group would do so.

Conclusion: This preliminary data suggests that many women physicians postpone important life decisions in pursuit of their medical career. While it does not appear that there were differences in relationship status between groups, the data indicates there may be an association with decision deferment and career specialty as well as career satisfaction. Overall, interesting correlations surrounding the work-life balance of women physicians may exist, and once our data is complete we expect to present more definitive conclusions with more variable comparisons.

Alarm Fatigue: Characterization and reduction of nuisance alarms

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Background: Excessive number of clinically insignificant or “nuisance” alarms can create a sensory overload in first line healthcare workers, often termed alarm fatigue. Alarm fatigue can result in missed alarms, increased time to respond to an alarm, and at times compromise patient safety and increased morbidity and mortality. There are little data on how best to reduce alarm fatigue.

Objective: The goals of this quality improvement initiative were: to categorize alarms based upon the associated hazard; determine the variables responsible for alarms; and to customize alarm parameters to reduce the number of nuisance alarms without compromising patient safety.

Methods: All alarms throughout the hospital were recorded and analyzed based upon the location and type of alarm. A multidisciplinary team developed a process that categorized alarms based upon their priority for patient risk and customized new alarm parameters.

Results: There were an average of 23,428 alarms across the hospital in a 24-hour period.

14,044 (60%) of these alarms were from adult and neonatal ICU units. There were 3951 (16.8%) alarms from telemetry devices throughout the hospital. Of the 23,428 alarms 11,907 (50.8%) alarms were caused by physiologic changes: heart rate (2237, 13.3%); respiratory rate (1182, 7.0%); and SpO₂ (1844, 11%). We will implement changes to the default parameters of devices to not alarm: Changing default lower and upper heart rate limits (40-140); default lower respiratory rate equal to 9; and default lower SpO₂ 88%. These changes to the physiologic defaults can lead to the elimination of 5263 (44.2%) of the physiologic alarms. Similarly, we can eliminate alarms for run PVC (101, 0.6%), pair PVC (1345, 8.0%), R-on-T PVC (50, 0.3%), PVC/min (417, 2.5%), multiform PVC (981, 5.8%), pacemaker not captured or pacemaker not pacing (24, 0.2%), missed beats (353, 2.1%), and irregular heart rate (541, 3.2%). The remaining 11,521 alarms were considered to be high priority clinically relevant. The small changes in the alarm parameters of telemetry devices is expected to reduce total alarms in the hospital by 9075 alarms (54%).

Conclusion: There are a large number of alarms that do not indicate physiologic changes in vital signs. By customizing the default parameters of telemetry devices the number of alarms can be reduced without compromising patient safety and improve quality of care.

Laser Treatment and Reversal of a *C. elegans* Model of Human Neuromuscular Degenerative Disease

TsungYen Chen, Dmitry A. Nedosekin, Leslie K. Climer, James Cooper, Vladimir P. Zharov, Srinivas Ayyadevara, and Robert J. Shmookler Reis

Neuromuscular degenerative diseases are common and can be associated with aging but often have significant genetic predispositions. Some of these diseases are characterized by abnormal protein aggregations, *e.g.* polyglutamine (polyQ) clusters in Huntington's disease and beta amyloid ($A\beta_{1-42}$) plaques in Alzheimer's disease. In this investigation, the AM141 strain of the nematode *C. elegans*, which forms intramuscular polyglutamine aggregates (Q40) coupled to a yellow fluorescent reporter protein (Q40::YFP), served as the model organism for progressive intracellular protein aggregation accompanied by declining motility. With photothermal ablation of these aggregates guided by fluorescent signals, we were able to significantly prolong the lifespan of diseased nematodes by 40% ($p < 0.003$) and preserve their motility by delaying degradation of muscular functions. The results from this investigation are applicable to interstitial or transcutaneous delivery of laser treatments to human tissues and organs, reversing similar intracellular aggregates that occur in various locations.

Genotype-phenotype study of patients with valosin-containing protein (VCP) multisystem proteinopathy

First Author: Ebba Al-Obeidi Tahseen Mozaffar, MD, Abhilasha Surampalli, MBBS, Namita Goyal, MD, Charles Smith, MD, Molly Omizo, MD, Darrel Waggoner, MD, Virginia Kimonis, MD

Missense mutations in valosin-containing protein (VCP) lead to VCP disease: limb-girdle/inclusion-body myopathy (IBM) associated with Paget's disease of bone (PDB), frontotemporal dementia (FTD), and amyotrophic lateral sclerosis (ALS). VCP is an ATPase found in all cells and is a key player in protein degradation and autophagy. VCP disease is a progressive, lethal disorder that has an autosomal dominant adult onset. To date, 44 disease-causing mutations in the VCP gene have been reported worldwide. The goal of this study was to examine genotype-phenotype data from 231 individuals (118 males, 113 females) from 36 families carrying 15 different VCP mutations (three of which are novel), this cohort representing the largest cohort published to date. We analyzed whether the different mutations were related to age of onset and severity of IBM, PDB, and FTD, and measured the prevalence of those conditions and other comorbidities. We ultimately found that the R159C mutation led to a significantly later age of onset of myopathy. Myopathy was present in 89% of the patients, beginning at an average age of 43 years. PDB was diagnosed in 43% of patients with an average age of onset of 41 years. FTD presented in 29% of the individuals at an average age of 56 years. Approximately 9% of patients with VCP mutations had an ALS phenotype, 4% had been diagnosed with Parkinson's disease, and 2% had been diagnosed with Alzheimer's disease. By understanding the typical clinical presentation and age of onset of symptoms, clinicians will be better able to diagnose VCP-related diseases and to manage patients more effectively.

Closed-Loop Glucagon Administration for the Automated Prevention and Treatment of Hypoglycemia in Type 1 Diabetes

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Introduction: For patients with type 1 diabetes, maintaining blood glucose (BG) values near a normoglycemic range has been shown to reduce long-term diabetic complications. However, with more tightly regulated BG control, there is also an increased risk for hypoglycemia which can result in seizures, coma or even death. Fear of these life-threatening complications is a major barrier to optimal glycemic control. While an emergency glucagon injection is currently the standard treatment for severe hypoglycemia, we propose that automated administration of microdose glucagon via a closed-loop bionic pancreas system will be effective at reducing the incidence and severity of hypoglycemia in patients with type 1 diabetes.

Methods: 22 adult patients from Massachusetts General Hospital were enrolled in a two-week, randomized, crossover outpatient study. Criteria included self-reported frequency of documented hypoglycemia or a history of hypoglycemic unawareness. During this time, participants administered insulin in their usual care fashion while receiving either glucagon or placebo (randomized, 7 days of each) through a closed-loop bionic pancreas system. This system consisted of a continuous glucose monitor (CGM - Dexcom G4), an iPhone 4S housing the control algorithm, and an infusion set connected to a Tandem t:slim pump. The primary outcome was the area over the CGM glucose vs. time curve that fell below 60 mg/dl (AOC_{60}), a measure of both hypoglycemic duration and severity. Paired t-tests were used for comparison of means between glucagon and placebo days.

Results: Among the 22 participants, there was a significant reduction in mean AOC_{60} on glucagon vs. placebo days (878 ± 768 vs. 3414 ± 2242 (mg/dl) · min, $p < 0.0001$). Additionally, there was a reduction in mean percentage of time spent with a CGM glucose level below 60 mg/dl on days patients received glucagon in contrast to placebo ($1.2 \pm 0.8\%$ vs $4.7 \pm 3.5\%$, $p < 0.0001$). No significant changes were observed in mean CGM blood glucose during the glucagon vs. placebo arm (154 ± 28 mg/dl vs 152 ± 27 mg/dl, $p = 0.5$).

Conclusion: This data suggests that microdose glucagon adjunct to open-loop insulin administration is an effective way to reduce the incidence of hypoglycemia without raising the mean BG. In comparison, as seen in our previous studies, a bihormonal bionic pancreas utilizing insulin and glucagon is able to reduce hypoglycemia while also decreasing mean BG to allow for tighter glycemic control.

Evaluation of a Physician Managed Weight Loss Program and Patients with Obesity

Michelle Dilley, Allen Felix

Introduction: The high prevalence of obesity coupled with physical inactivity has created a public health epidemic. Approximately two-thirds of U.S. adults are overweight (BMI 25-30) or obese (BMI \geq 30). These individuals are at increased risk for developing type II diabetes mellitus (DMII), hypertension (HTN), hyperlipidemia (HLD), and other conditions. To help address these issues, Felix Medical Group implemented the Cornerstone Wellness Weight Loss Program, which consists of high protein meal replacements. This study assesses the effectiveness of this physician managed weight loss program, weight perceptions, diet, and exercise for patients with obesity.

Methods: Data including BMI, concurrent health problems, and enrollment with a family member was collected for all patients participating in the weight loss program (n=56). After the initial consultation, patients began the Cornerstone Wellness Weight Loss Program. Patients were instructed to follow up in 2 weeks, again in another 2 weeks, and then on a monthly basis for repeat evaluation. Compliance scores and BMIs were recorded at each visit. Surveys to assess weight perception, program satisfaction, weight loss strategies, eating habits, and exercise were distributed to patients during a 3-week span.

Results: Of the 56 patients participating in the weight loss program, 20 have been active for >3 months (mean BMI=38.8, SD=6.5). Many of these patients presented with comorbid conditions (HTN=55%, DMII=40%, HLD=60%) and 45% enrolled with a family member. Of these 20 patients, 6 experienced overall BMI decreases >2 (Mean BMI decrease=3.6, SD=1.4). All 6 of these patients had above average compliance scores and <2.5-month gaps in between follow up visits. The majority of surveyed participants expressed satisfaction with the program. Of the surveyed patients not participating in the weight loss program and with BMI \geq 30 (n=29), 76% did not perceive themselves as obese, 59% tried a weight loss program, and 69% did not usually eat breakfast. Additionally, most patients reported a lack of exercise due to limited time and energy.

Conclusion: The Cornerstone Wellness Weight Loss Program implemented at Felix Medical Group is clinically useful for decreasing BMI in certain overweight and obese patients. Patients with higher program adherence experienced larger BMI decreases compared to less compliant patients. The majority of patients with obesity inaccurately perceived their weight, had unhealthy eating habits, and lacked exercise. Felix Medical Group is further educating patients about BMI and encouraging lifestyle modifications to help reduce obesity and associated comorbidities. Future directions involve assessing readiness for change and offering different weight loss options to create a more personalized approach for patients with obesity.

The Role of Technology in the Medication Cost Conversation

Margarita Ivanova, BA Tahira Adaya, BS Sivakami Sambasivam, BS Sharon Orrange, MD, FACP

Introduction: Medication nonadherence is estimated to cost the U.S. Healthcare system \$290 billion a year. The inability to afford medications is the most consistent reason stated by patients for medication nonadherence. Despite this, the conversation between patient and physician about medication costs is often lacking or non-existent. The main barriers to discussing medication cost by physicians are insufficient time, patient discomfort, lack of habit, and lack of solution.

New technology improves transparency and access to prescription drug costs, alleviating many of these stated barriers to communication. GoodRx, a website and mobile app, is an aggregator of medication cost information that receives over 4 million visits per month. It allows users to enter their zip code and compare prices of prescription medications at their local pharmacies.

Little is known about whether such online price transparency improves medication adherence or facilitates patient-physician communication about drug cost. This study examines the impact of cost savings from GoodRx on medication adherence and the role of GoodRx in improving patient-physician communication regarding prescription drug cost.

Methods: We administered a survey to users of the website GoodRx (www.GoodRx.com). Data were collected over a five day period in November 2015. Descriptive statistics were used to characterize survey responses.

Results: Overall, 1385 people completed the survey. The mean age of respondents was 62 with women comprising 54% of the sample. Overall, 80% had medical insurance, with 52% of those having Medicare. Surprisingly, 86% of respondents found their medication for less with 69% reporting they were more likely to take their medication because of those savings. Nearly 60% reported that their physician had never discussed medication cost with them and only 18% were directed to the site by a physician. Of the nearly 1,200 respondents who found their medications for less, 44% discussed those savings with their doctor. While most participants (52%) reported no change in their patient-physician relationship after discussing savings gleaned from GoodRx, 47% reported a positive impact on the relationship. Gender and years in practice showed no significant differences in whether or not the physician had discussed medication cost with the patient.

Conclusions: The inability to afford medications is a crucial factor in medication nonadherence. Novel websites and mobile apps, such as GoodRx, provide medication cost transparency and significant savings. In doing so, they may play a key role in improving medication adherence and alleviating barriers to the patient-physician medication cost

conversation. This has the potential to improve patient care through better patient-physician communication and to thus enhance quality of care.

Multiple Hypoglycemic Events in Hospitalized Patients

First Author: Emily Johnson, MPH Daniel DeMoss MD, Nima Tehari MD, Christopher Pham BS, Amy Komura BS, Gina Rossetti MD

Importance: Hypoglycemic episodes in hospitalized patients represent a major concern among healthcare professionals as these events are associated with adverse patient outcomes including increased hospital stays, healthcare costs, and mortality.

Objective: Determine the characteristics and risk factors of recurrent hypoglycemic episodes in non-critically ill inpatients.

Methods: A review of the LAC-USC electronic medical record was conducted for all recorded serum glucose values <70mg/dl occurring from July 1, 2012 to July 31, 2013 on adult non-ICU medical/surgical floors (n=2,197 events). Characteristics of patients with single vs. multiple events and patients with concurrent point-of-care fingerstick (POC) glucose monitoring vs. those unmonitored were compared using models adjusted for age, sex, renal function, diabetes, and presence of any malignancy as well as assessing for NPO status. We excluded patients on total parenteral nutrition.

Measures: Multiple hypoglycemic episodes, as measured on serum blood draw. We also examined the events occurring in the POC-monitored and unmonitored populations. All-cause mortality, as documented death during the hospital stay or a discharge to hospice care.

Results: The 2,197 hypoglycemic events occurred in a total of 1,144 individual adult patients. Of these, 360 patients (31.3%) had more than one hypoglycemic event in a single admission and were more likely to have metastatic disease, diabetes, higher mean creatinine, lower blood glucose, on insulin therapy, or be NPO. Mean length of stay in participants with multiple events was 20.0 days (sd=28.6) compared with mean stay of 11.9 days (sd=16.3) with a single hypoglycemic event, ($p<0.05$). Among patients who were not on POC monitoring (n=723, 63%), renal failure, cancer, and NPO status were significantly associated with multiple hypoglycemic events [OR=1.67 (95%CI: 1.05-2.64), OR=1.62 (95%CI: 1.10-2.37), OR=1.65 (95%CI: 1.15-2.30), respectively]. These associations were not significant among patients on POC monitoring. In a similarly adjusted model examining association with mortality, multiple hypoglycemic events were associated with twice the odds of mortality OR=1.99 (95%CI: 1.28-3.10), and POC monitoring with decreased mortality, OR=0.57 (95%CI: 0.35-0.93).

Conclusions: Among adult patients on medical/surgical floors, multiple hypoglycemic events were associated with increased length of stay. Additionally, patients with multiple hypoglycemic events on serum draw were those with renal failure, NPO orders, or cancer, and would not normally be monitored using POC testing. Further examination of monitored vs. unmonitored patients showed these risk factors were only significant among the unmonitored, suggesting there may be important differences in care reducing multiple hypoglycemic episodes in patients who are receiving POC monitoring. We are currently initiating an intervention using POC glucose monitoring for inpatients with renal failure, cancer, and NPO status, examining hypoglycemic episodes, time to corrective action, and mortality.

Prevention of Hepatitis B Virus Reactivation: Are Patients Appropriately Screened Prior to Rituximab Treatment?

Kevin Junus, Maria Aguilar, Priya Patel, David Irwin, Stephen Yee, Benny Liu, Taft Bhuket, Robert J. Wong

Background: Hepatitis B Virus (HBV) is a leading cause of chronic liver disease worldwide, with over 240 million people chronically infected. Among individuals with chronic HBV or with previously resolved HBV infection, immunosuppression increases the risk of acute HBV exacerbation or reactivation, with up to 40% experiencing reactivation with anti-CD20 therapies, such as rituximab (RTX). Mortality associated with HBV reactivation can be as high as 25%. Effective screening for past or current HBV infection among patients undergoing anti-CD20 therapy will help guide appropriate initiation of antiviral therapy to prevent morbidity and mortality associated with HBV exacerbation and reactivation.

Aim: To evaluate rates of appropriate HBV screening prior to initiating RTX therapy.

Methods: We performed a cross sectional study evaluating all consecutive adult patients treated with RTX at Highland Hospital from 2006 to 2015. We defined appropriate screening as evaluation of both HBV surface antigen (HBsAg) and HBV total core antibody (HBcAb) prior to initiation of RTX. Appropriate screening rates were stratified by sex, race/ethnicity, and year of treatment initiation. Comparison of appropriate screening rates between groups utilized chi square testing, and a two-tailed $p < 0.05$ was considered statistically significant.

Results: Overall, 244 patients received RTX treatment from 2006-2015. The majority of our cohort was female (52.7%, $n=128$), and the predominant race/ethnic group was Hispanic (30.7%, $n=74$). Overall, 75.7% ($n=184$) of patients were screened for HBsAg, 61.3% ($n=149$) were screened for HBcAb, and 60.5% ($n=147$) were screened for both. When stratified by year of treatment initiation, rates of appropriate HBV screening prior to RTX demonstrated significant improvements, from 14.7% in 2006-2009 to 74.7% in 2010-2012 and 87.1% in 2013-2015. When stratified by race/ethnicity, Hispanics were more likely to receive appropriate HBV screening, whereas Asians were less likely to receive appropriate HBV screening (non-Hispanic whites: 64.9% vs. blacks: 60.9% vs. Hispanics: 70.3% vs. Asians: 51.9%, $p=0.014$). Among 4 patients screened positive for HBsAg prior to RTX, 1 started antiviral treatment and 33.3% ($n=1/3$) who was not treated with antiviral therapy experienced HBV flare and died. Among 32 patients screened positive for HBcAb, 6 started antiviral therapy, and 3.8% ($n=1/26$) not started on antiviral therapy experienced HBV reactivation. Of the 93 patients not appropriately screened for both HBsAg and HBcAb, 2 patients (2.2%) experienced HBV reactivation and were found to be HBcAb positive.

Conclusions: Among adults receiving RTX therapy from 2006 to 2015, only 60.5% received appropriate screening for HBV. However, rates of appropriate HBV screening during our study period improved by nearly 5-fold, and in 2013-2015, nearly 90% of patients were appropriately screened. Rates of initiating antiviral therapy among patients with positive HBsAg or positive HBcAb remained low. Better awareness of HBV reactivation is necessary among providers to achieve improved screening rates and subsequently initiate prophylactic treatment as appropriate prior to RTX therapy in order to prevent complications of reactivations including fulminant liver failure and death.

Development of a Clinical and Translational Research Pathway at the David Geffen School of Medicine at UCLA

Emily Miller, Christina Harview, Lyudmyla Deyman, LuAnn Wilkerson, Isidro Salusky

Many medical schools in the United States do not have a research component or emphasis on research within their curriculums. Yet, there is an increasing need for physician-scientists and clinicians with a solid foundation in research training. In response to this shortage, the David Geffen School of Medicine at University of California, Los Angeles (DGSOM at UCLA) has created the Medical Student Pathway in Clinical and Translational Science. This elective program is longitudinal over the four years of medical school, and allows students to receive support and training in research without taking time off from medical school. The goal of the pathway is to provide students who are interested in research with access to high quality mentors and scholarly opportunities that emphasize the transition of scientific knowledge from bench to bedside. The first 19 students to successfully complete this pathway have cumulatively published 62 scientific publications during their time in medical school. Additionally, these 19 students completed a Pathway entrance and exit survey, demonstrating that students found benefits in the pathway including assistance finding a research mentor, having the chance to discuss research at residency interviews, and being able to publish their research results. Students in the pathway showed a dramatic increase in their understanding of scientific process including operationalizing a research question, choosing an appropriate research design, and running statistical analyses. Assessment of these outcomes provides valuable information on the successes of the pathway and sheds light onto what aspects of the program can be further developed. The elective Medical Student Clinical and Translational Research Pathway has so far proven to be an excellent model for the training of physician-scientists and should be considered a viable option for addressing the increased demand for clinicians with experience in empirical research.

Analysis of Risk Assessment Tools for Readmission

First Author: KimNgan Nguyen Second Author: Dwight Miller MD Third Author: Sitaram Vangala MS Fourth Author: Erin Dowling MD

Background: Many hospitals are adopting risk assessment tools to identify patients at high risk for readmission, in order to lower 30-day readmission rates and avoid a readmission penalty recently placed by the Center of Medicare Services. While these models have proven to be useful for other health systems, no tool has yet been adopted by the Internal Medicine Service at Ronald Reagan UCLA Medical Center. The aim of this study is to assess the use of different readmission prediction tools and determine which is most accurate and helpful for predicting readmissions. Specifically, we compare the LACE score with physician, nurse, and case manager gestalt.

Methods: We surveyed providers on the Internal Medicine Service at our academic hospital, asking them to assess patients' readmission risks and to identify potential factors associated with increased readmission risk. Providers estimated risk for each patient on a continuous scale from 0 to 100 percent. Each patient was tracked for readmission for 30-days after the date of discharge. Actual readmission rates were compared to providers' predictions of readmission rates. The LACE score was calculated for each patient prior to discharge. Receiver operator curves (ROC's) were constructed for each provider group and the LACE index to further characterize the predictive power of the different tools.

Results: Residents, attendings, nurses, and the LACE score were all able to distinguish readmitted from non-readmitted patients. The mean LACE index for readmitted patients was 11.4, compared to 9.9 for non-readmitted patients ($p = 0.006$). Residents, attendings, and nurses all predicted higher mean risk of readmission for readmitted compared to non-readmitted patients ($p < 0.05$). When analyzed with ROC's, resident gestalt was the most accurate predictor of readmission, followed by attending gestalt, nursing gestalt, and LACE index. Subgroup analysis showed that different provider groups had better predictive abilities based on the clinical characteristics of the patient.

Conclusion: Our data shows that the mean LACE score was high for our patient population, and the difference between the LACE score for readmitted and non-readmitted patients was small, in spite of its statistical significance. Additionally, our study shows that residents, attendings, and nurses were able to significantly distinguish between readmitted and non-readmitted patients, and out-performed the LACE index when analyzed with ROC's. Based on these results, we are exploring how to incorporate provider predictions into discharge planning at our institution.

Reduction in Infection Rates of Multidrug-Resistant Microorganisms Following Adoption of Daily Patient Washing with 2% Chlorhexidine Gluconate

First Author: Amisha Patel-Oza, BA, BSN, MSN Second Author: Avinash Oza, BS Third Author: Sibte Burney, MD Fourth Author: Steven Brooks, PhD

Hospital acquired infections (HAIs) caused by multidrug-resistant microorganisms (MDROs) place a significant financial and ethical burden on health care institutions. Two million people are infected by MDROs annually, leading to 23,000 deaths. Review of recent publications show that patient bathing with chlorhexidine gluconate (2% CHG) reduced central line infections, particularly those caused by MRSA in high risk settings.

We report on the results of an interventional study, where daily patient bathing with cloths impregnated with 2% CHG was incorporated into standard patient care practice to achieve universal decolonization of skin flora. The study was conducted on three high-risk units (ICU, CCU, and a ventilator unit) in a 303-bed community medical center. MDRO infection rates (cases/1000 patient days) were assessed for 577 days before and 577 days after the implementation of daily CHG washing. MDROs reviewed in this study include resistant strains of Klebsiella, Pseudomonas, Acinetobacter, E. coli, and Enterobacter, as well as Clostridium difficile, MRSA and vancomycin resistant Enterococcus (VRE). Central line associated bloodstream infections (CLABSI) and carbapenem resistant Enterobacteriaceae (CRE) strains were also investigated.

Patient days for pre and post intervention periods were similar (18,490 versus 16,918). There were 106 MDRO HAIs noted pre-intervention, and 38 infections post-intervention. Overall MDRO infection rates were 5.73 pre-intervention versus 2.25 post-intervention (-60.8%).

Pathogen specific pre and post-intervention infection rates were as follows: Klebsiella, 1.57 versus 0.47 (-69.9%); Acinetobacter, 1.30 versus 0.18 (-86.3%); VRE, 0.59 versus 0.12 (-80.1 %); MRSA, 1.51 versus 0.77 (-49.3%); Pseudomonas, 0.22 versus 0.12 (-45.4%); C. difficile, 0.43 versus 0.41 (-4.4%). The minimal effect of CHG on C. difficile infections may be explained by CHG's inability to kill infectious C. difficile spores. CRE is a contemporary epidemiologic concern. The rates of carbapenem resistant Klebsiella, E. coli and Enterobacter infections were significantly reduced by CHG, yielding 1.30 pre-intervention versus 0.41 post-intervention (-68.1%). CLABSI infections were also reduced following CHG intervention. The rates of CLABSI by unit were: CCU, 1.03 versus 0.40 (-61.7%); ICU, 1.86 versus 0.76 (-58.8%); ventilator unit, 1.37 versus 0.61 (-55.7%).

Our confirmatory study supports and expands upon prior research, involving the efficacy of decolonization using CHG to reduce HAIs in high-risk patients. Given the promising results of this study, as well as those in the literature, daily patient washing with CHG has the potential to be a standard protocol in inpatient units to prevent HAIs caused by MDROs.

Mesenchymal Stem Cells for Treatment and Prophylaxis of GVHD: A Systematic Review of Clinical Trial Heterogeneity

Background: Graft versus host disease (GVHD) is a significant complication following allogeneic hematopoietic stem cell transplantation (HSCT) and is associated with increased morbidity and mortality and is affected by many patient and treatment conditions. The frontline treatment for GVHD is immune suppressive therapy, with glucocorticoids being the preferred option. However, only about half of patients respond to therapy and there is no clear second-line therapy for these steroid-refractory cases. One treatment that has shown promise is mesenchymal stromal cells (MSCs). MSCs are a pluripotent cell population that may be isolated from many tissues in the human body including bone marrow, adipose and placenta, and can differentiate into cell lineages of mesenchymal origin. Many phase I and II clinical trials have been performed examining the use of MSCs for GVHD, but the results are ambiguous with regard to benefits in patient outcomes. This ambiguity may be due to the broad heterogeneity that exists across these studies with regard to patient population, treatment regimen and the MSCs being administered. It would therefore be timely to perform a systematic review to characterize and attempt to quantify this heterogeneity.

Methods: We performed a search to identify studies in MEDLINE, EMBASE and PUBMED databases. The search strategy was peer-reviewed by a medical information specialist. We included all interventional and retrospective clinical studies describing the use of MSCs or MSC-derived products, regardless of outcome, in human patients for the treatment or prevention of aGVHD and/or cGVHD. Titles and abstracts of studies identified by the systematic search were screened for relevance by two independent investigators. Relevant articles identified through the screen were reviewed for complete assessment of eligibility criteria. Discrepancies were resolved through consensus. Studies where GVHD was a primary outcome were further classified based upon whether MSCs were given for the prevention or treatment of GVHD. Data was manually extracted using Distiller SR[®] software.

Results: 70 studies were identified through the search, with 30 of these studies being clinical trials with GVHD as a primary outcome. We found significant heterogeneity between these studies with regard to patient populations being studied and the MSCs being administered. Patient populations were quite different with regard to diagnosis, stem cell product, donor, GVHD severity and conditioning regimen. MSCs varied in their source, expansion media, media supplement, and degree of characterization. No studies fully met ISCT criteria for *bona fide* MSCs.

Conclusions: Studies examining MSCs for the treatment or prevention of GVHD are quite variable and it is therefore difficult to draw a conclusion of consensus from the body of evidence with regard to the efficacy of MSCs for GVHD. It is imperative that future, larger, and controlled studies be performed with a rigorous and consistent study design.

Primary Care Providers Are Vital to Carrying out Hepatitis C Screening

First Author: Daniel Gaballa, BS, Shreya Chablaney, BS, Justin Ertle, MD, Timothy Dougherty, MD, Marie L. Borum, MD, EdD, MPH

Background: Chronic Hepatitis C Virus (HCV) infection affects approximately 3 million Americans. The 1945-1965 birth cohort has the highest prevalence, estimated at 2%. In 2013, the United States Preventive Services Task Force (USPSTF) endorsed screening for HCV in this cohort with the goal of identifying cases and initiating treatment. However, a variety of obstacles to screening are suspected to contribute to low screening rates. This study evaluated the role of the primary care physician in completing recommended screening in an historically underserved community with a high prevalence of HCV.

Methods: Individuals attending an August 2015 health exposition sponsored by the Rodham Institute completed an anonymous survey. The exposition was hosted in an urban setting where the population has historically been predominantly African American; currently 92% of residents identify as such. The survey included questions on demographic information, access to a PCP, insurance status, as well as knowledge of various topics related to Hepatitis C. Responses were excluded if they did not provide information on their history of screening. The university institutional review board approved the study. Statistical analysis was performed using Fisher's exact test, with significance set at $p < 0.05$.

Results: Ninety five responses were analyzed. Among them were 29 born in the 1945-1965 timeframe. All of members of this cohort reported having a primary physician and 27 (96.4%) had health insurance. Sixteen discussed HCV with their doctor and 12 of them (75.0%) were screened. Thirteen respondents had not discussed HCV; among them, three (23.1%) were tested for the virus. Having a discussion with the primary physician resulted in a significantly higher rate of HCV screening ($p = 0.0092$).

Conclusions: The primary care provider is vital to implementing preventive health recommendations including those related to HCV screening. Our study showed that in a high-prevalence, insured cohort, patients who had discussed HCV with their primary physician were three times more likely to have been screened for the infection. The population studied all had health insurance and a primary care provider, so health care was broadly accessible. The study also suggests that some recent USPSTF guidelines may not have penetrated into community primary care practices as the screening rates were suboptimal.

Elevated Body Mass Index Associated with Early Total Knee Revision

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Background: Obesity adversely affects perioperative morbidity and mortality after total knee arthroplasty (TKA). However, it is unknown whether higher-than-normal body mass index (BMI) affects survivorship of knee implants. The primary outcome measure was knee implant survivorship. A secondary outcome measure was to determine whether increased BMI was associated with a specific complication requiring revision TKA.

Methods: Using the total joint registry of our institution, we retrospectively reviewed 666 revision TKAs performed in 642 patients from 2005-2014. Age, gender, reason for revision TKA, pre-operative BMI, and time from primary to revision TKA in years were identified. Patients were eligible for analysis if they had a revision TKA performed at our center. 680 TKAs (656 patients) were initially selected for retrospective analysis. Patients were excluded if they did not have a date of primary surgery, preoperative BMI, or a minimum of one year of follow-up.

Results: A significant difference in survivorship between patients with a BMI between 30-35 kg/m² and patients <25 kg/m² was found ($p=0.005$, after Bonferroni correction). A significant difference in survivorship between patients with BMI <25 kg/m² and >25 kg/m² was also found ($p=0.005$, after Bonferroni correction). There was no significant difference in the rate of aseptic loosening/osteolysis, infection, instability, stiffness, and other causes of revision TKA at any time interval between BMI <25 kg/m² and >25 kg/m² ($p > 0.001$ after Bonferroni correction).

Conclusions: We are the first to document an earlier time to revision for TKAs in patients with an elevated BMI. Survival analysis showed that there was significant difference between patients with normal BMI (<25 kg/m²) and obese class II (35-40 kg/m²) patients, as well as normal BMI and higher-than-normal BMI. Additionally, we would argue that the fact that the only significant difference in BMI groups was between normal and obese class II is likely evidence of a larger trend than of an isolated result. The comparison between normal (<25 kg/m²) and obese class I (30-35 kg/m²), narrowly missed significance but suggests a strong trend especially in the setting of rigorous statistical analysis involving a Bonferroni correction. The implication of these results is that overweight patients and obese patients as an aggregate may have early implant failure compared to patients with normal BMI, but no specific complication can be correlated to early implant failure. Orthopaedic surgeons should urge overweight as well as obese patients to lose weight prior to TKA to enhance knee implant survival.

Halting the Boomerang: Hospitalizations, Readmissions, and Emergency Department Use of Patients in a Transitional Care Clinic

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Introduction: Thirty-day readmissions (30dR) cost over \$17 billion annually. The Affordable Care Act calls for penalization of hospitals with high 30dR rates, spurring interventions to address this issue. One such intervention is the transitional care clinic (TCC), which bridges medical coverage between the hospital and primary care.

Objectives: Reduce hospitalizations, 30dRs, and ED visits for discharged patients through intervention of establishing care at a TCC.

Methods: Retrospective chart review was done for 41 out of 300 Athens Regional Medical Center TCC patients (65.9% male, 48.80±12.95 years old). Mean numbers of hospitalizations, 30dRs, and ED visits were calculated for equal time periods before and after first TCC visit, based on how long the subject had been a patient at the TCC. Data were analyzed using a t-test.

Results: Mean number of pre-intervention hospitalizations per patient was 0.878±0.249, decreasing to 0.439±0.336 post-intervention (p=0.0024). Mean number of pre-intervention 30dRs per patient was 0.122±0.156, increasing to 0.171±0.204 post-intervention (p=0.421). Mean number ED visits per patient fell from 1.829±0.479 pre-intervention to 1.390±1.145 post-intervention (p=0.314).

Conclusion: TCC attendance had mixed effects on healthcare use, showing significantly reduced hospitalizations but no significant differences in ED visits or 30dRs. These results are clinically relevant because patients established care that allowed for detection and management of disease.

Survivorship in Patients with Small-Cell Lung Cancer Receiving Prophylactic Cranial Irradiation

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Background: Small-cell lung cancer (SCLC) is a highly aggressive malignant tumor of neuroendocrine cells that accounts for 13% of all lung cancers diagnosed in the United States. Approximately 75% patients are found to have metastasis at diagnosis; for these patients, 2-year survival is 4.6%. Of the most common sites of metastasis, brain involvement carries the worst prognosis. Prophylactic cranial irradiation (PCI) is an established intervention for patients without evidence of brain metastasis at the time of original diagnosis. This intervention has come under criticism recently and its benefit in the community setting has not been previously studied. We assessed the survival benefit of PCI in the largest population of patients treated in the community setting to date.

Methods: 236 patients with SCLC were managed at a major community hospital between 1990 and 2014. Demographics and survival data were retrieved from electronic medical chart under an IRB-approved protocol. Overall survival was calculated from time of original diagnosis to date of documented death using the Social Security Death Index. Survival plots were generated by Kaplan-Meier methods for patient subgroups treated with and without prophylactic cranial irradiation (PCI). Incidence of brain metastasis in patients treated with or without PCI was assessed.

Results: We employed data available in a total of 112 patients for this analysis. There were 54 females (48%), the median age at diagnosis was 59, and the racial breakdown included blacks (91%) and caucasians (9%). 21 (18.6%) patients received PCI while 91 (81.3%) did not. The median overall survival for the PCI-treated group was 26.2 months (95% CI: 16.8 to 41.39), compared to 8.38 months (95% CI: 6.21 to 9.96) for the group not treated with PCI. The incidence of brain metastasis was 14.3% (3/21) in the patients who received PCI and 47.3% (43/91) in patients who did not receive PCI.

Conclusions: Consistent with registry database analysis and prospective randomized studies, PCI was associated with reduced incidence of brain metastasis and improved overall survival in patients with small-cell lung cancer treated in a community hospital setting.

Clinicopathological Significance of Tumor Suppressor Genes MMR and ARID1A in Endometrial Intraepithelial Neoplasia

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BACKGROUND: Endometrial intraepithelial neoplasia (EIN) is a hyperplastic premalignant lesion to type 1 endometrial carcinoma. Endometrial cells have high rates of cellular turnover that increase risk of somatic mutations such as hypermethylation of mismatch repair (MMR) and loss of tumor suppressor gene ARID1A. MMR normally serves as quality control during DNA synthesis, and MMR deficiency can lead to tumor development. In endometrial carcinoma, MMR deficiency is strongly associated with somatic mutations of ARID1A, a tumor suppressor gene. Controversy remains as to whether ARID1A loss of expression is the cause or result of MMR deficiency in endometrial carcinoma, and only two small-scale studies have analyzed the association of its precursor EIN with ARID1A loss of expression. Both studies found significant correlation between these two events. Clinical implications include screening for high risk patients and potential gene-targeted therapy.

OBJECTIVES: This is a retrospective study of MMR and ARID1A expression in defined EIN. The purpose is to determine the incidence of MMR and ARID1A mutations in defined EIN in one of the largest series yet published. Furthermore, this study will analyze the correlation of MMR with ARID1A.

METHODS: Endometrial biopsies were performed on 113 women. Immunohistochemical staining was used to indirectly measure gene mutation and subsequent loss of expression (LOE). A two-tailed Fisher exact test was performed, with significance defined as p-value <0.05.

RESULTS: The rate of ARID1A LOE (6.2%, n=7/113) was slightly greater than the rate of MMR LOE (4.4%, n=5/113). There was no significant difference between ARID1A expression and MMR expression (ARID1A retained/MMR LOE n=5/113, ARID1A LOE/MMR retained n=7/113, p=1.000). Furthermore, there was neither significant difference between ARID1A expression and subsequent cancer (ARID1A retained/no subsequent cancer n=26/55, ARID1A LOE/subsequent cancer n=4/55, p=0.1135) nor significant difference between ARID1A expression and subsequent cancer stage (ARID1A retained/Stage I n=49/55, ARID1A LOE/greater than Stage I n=1/55, p=0.2062).

CONCLUSION: In 113 cases of defined EIN, the incidence of MMR LOE (4.4%) and ARID1A LOE (6.2%) was surprisingly low. Contrary to two small-scale studies, there was no significant association between expression of MMR and ARID1A in EIN. Considering there is an established correlation between MMR LOE and ARID1A LOE in endometrial carcinoma, these findings suggest independent pathways or time-dependent changes in gene expression. This theory is supported by studies in gastric carcinoma that argue MMR and ARID1A are independent pathways. According to this study, MMR and ARID1A in EIN are poor predictors of subsequent endometrial carcinoma, and thus additional research is needed with respect to the pathogenesis of EIN and endometrial carcinoma.

A scaffolding protein, IQGAP1, is crucial to protect the liver from injury

Hanna Erickson, Karen Wendt, Sayee Anakk

Introduction: Liver disease affects approximately 1 in 10 Americans. A majority of liver diseases, including cirrhosis and hepatitis B and C infections, lead to liver dysfunction along with increased bile acid levels. Bile acids are amphipathic molecules in the liver that necessitate homeostatic regulation, since excess levels will result in necrosis. However, bile acids also function as signaling molecules and have been implicated in promoting liver proliferation. But how bile acids coordinate this process is not fully understood. Previously, we found that *Fxr*^{-/-}*Shp*^{-/-} mice, which have lost their feedback regulation of bile acid synthesis, develop early-onset cholestasis. Unexpectedly, these mice, as well as bile acid-fed wild-type mice, displayed a dramatic increase in hepatic expression of IQGAP1, a scaffold protein that has been shown to integrate various signaling pathways including those involved in proliferation. Moreover, bile acid-fed *lqgap1*^{-/-} mice display fewer proliferating liver cells than wild-type mice as indicated by Ki-67 staining suggesting a crucial role for IQGAP1 in promoting bile acid-induced proliferation. Interestingly, IQGAP1 is also overexpressed in human biliary disorder patients. Based on our results, we hypothesize that bile acids employ IQGAP1-mediated mitogenic signaling to promote liver proliferation.

Methods: Adult male wild-type 129SVJ and *lqgap1*^{-/-} mice were fed either a 1% cholic acid diet or a 0.1% 3,5-diethoxycarbonyl-1,4-dihydrocollidine (DDC) diet for 2 weeks. These diets represented mild and severe liver injury models, respectively. At the end of experiments, livers and serum were collected and flash frozen. Histological, biochemical, and gene expression analysis were then performed to examine the role for IQGAP1 in the response to injury.

Results: Bile acid feeding as expected resulted in modest injury and was able to mount a proliferative response. This response was IQGAP1-dependent such that *lqgap1*^{-/-} mice showed a 50% reduction in proliferative index. Therefore, we evaluated the expression of pro-proliferative (EGFR, ERK, B-catenin) and anti-proliferative signals (ILK, E-cadherin, phospho-SMAD3). Remarkably, only the anti-proliferative effects were mediated by IQGAP1 whereas the pro-proliferative effects were IQGAP1 independent. This indicates that IQGAP1, by inhibition of anti-proliferative signals, promotes cellular proliferation. Next, we decided to test this in a more severe model of liver injury using DDC. Wild-type mice treated with DDC showed robust induction of hepatic IQGAP1. We predict that the IQGAP1 induction in response to injury is important for the compensatory proliferative response. Consistently, *lqgap1*^{-/-} mice were not able to mount a proper response to the DDC-mediated injury precipitating with severe jaundice and cholangitis with bile lakes. These data suggest a protective role for IQGAP1 during liver injury.

Conclusion: IQGAP1 functions downstream of bile acids to promote proliferation in response to liver injury.

Hospital Horror Story: Situational Awareness to Assess Interns' Recognition of Hospital Hazards

Kathleen Wiest BS, Jeanne Farnan MD MHPE, Lukas Matern BS, Ellen Byrne MPP Candidate, Melissa Cappaert MA, Kristen Hirsch BSGS, Vineet Arora MD MAPP

Introduction: While many institutions train housestaff to mitigate hospital hazards, few have exploited the crucial concept of situational awareness (i.e. mindfulness of the patient environment) to teach patient safety. One method to promote situational awareness is through the embedding of hospital hazards into simulation-based training exercises. This study aims to assess incoming interns' ability to identify safety and low-value hazards of hospitalization in a simulation designed to promote situational awareness.

Methods: An inpatient simulation was constructed in collaboration with the University of Chicago Simulation Center as a required component of GME orientation. Incoming interns were given ten minutes to independently review a mock chart and list all hazards they identified in the simulated hospital room. Eight safety hazards (e.g. penicillin allergy) and four low-value hazards (e.g. unnecessary Foley catheter) were included in the simulation based on Medicare Hospital Acquired Conditions, AHRQ Patient Safety Indicators, and Choosing Wisely recommendations. Interns completed a short survey on their prior safety training in medical school, and a follow-up survey one month after beginning internship. Simulation performance was measured by the percentage of total hazards identified correctly. T-tests were used to compare safety versus low-value hazards and to associate performance with prior safety training.

Results: One hundred twenty-five interns (100% of those eligible) participated in the simulation, representing thirteen specialties and sixty medical schools. 73.5% (89/121) had received prior safety training in medical school, but only 50.0% (61/122) were satisfied with their prior training. The mean percentage of hazards correctly identified was 50.4% (median 50.0%, SD 11.8%). Interns identified significantly more safety hazards (mean 66.0%, SD 16.0%) than low-value hazards (mean 19.2%, SD 18.6%) ($P < 0.001$). There was no significant association between hazard identification and prior safety training or satisfaction with prior training. Interns entering less procedural-intensive specialties identified significantly more safety hazards (mean 69.1%, SD 16.9%) than those entering highly procedural-intensive specialties (mean 61.8%, SD 13.7%) ($P = 0.012$). One month post-simulation, 69% (82/119) of interns reported being more aware of how to identify hospital hazards, and 52% (62/119) had taken action to reduce a hazard that was included in the simulation.

Conclusion: Interns identified significantly more safety hazards than low-value hazards in the simulation. Prior safety training in medical school was not associated with interns' ability to detect hazards, and satisfaction with prior training was low. The simulation resulted in increased situational awareness leading to hazard mitigation one month into internship. This highlights the need for augmentation of experiential learning and situational-based training in medical education.

A year-round EBM learning course organized by medical students at Ehime University

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Introduction: According to the global standard medical school curriculum, evidence based medicine (EBM) is a scientific method which medical schools must teach throughout their curriculum. In contrast, opportunities to learn EBM in Japanese medical schools are not many. Therefore we, as medical students, organized a year-round scenario-based EBM-learning study course in 2014. There are some studies that showed the effectiveness of short term EBM learning courses organized by faculties or medical students. However, the effectiveness of year-round learning course organized by medical students was unknown. The objective of this study was to objectively evaluate the participants' understanding of keywords related to EBM.

Methods: This study was a prospective observational study of educational intervention at Ehime University. The outcome was the participants' understanding of keywords related to EBM. We conducted surveys three times by using an original survey with 23 questions related to participants' understandings or motivation. Each question was scored from 1 to 5, with 5 being the best understanding. Then we calculated the average scores of 19 questions related to the participants' understanding of EBM keywords, and measured how much the average score increased by between the first and the last survey. We also calculated the average score of the last survey by each questions to clarify which term the participants understood well. We used Wilcoxon Signed-Rank Test for calculation of the p value.

Results: Twelve classes were held from April 2014 to January 2015. Under the supervision of a medical doctor, students examined seven articles on randomized controlled trials (RCT), four on systematic reviews and meta-analysis, and one on understanding and practicing sensitivity and specificity. In total, 18 students responded to our survey. Of those 18 students, six students answered both the first and the last survey, and their mean score increased 1.17 out of 4.00 (95% CI: 0.72-1.65). The average score of the six samples on the last survey was significantly higher than the first survey ($p=0.028$). Assessing the last survey ($n=10$), the mean scores (minimum and maximum scores are 1 and 5) related to following words were high: randomization (4.2), withdraw (4.1), blind (4.2), relative risk (4.2), 95% confidence interval (4.4), sensitivity and specificity (4.1), while these words were low: clinical information tools (3.4), intention-to-treat analysis (3.2), meta-analysis (3.4) and heterogeneity (3.2).

Conclusion: Our course improved students' understanding of some keywords related to EBM. The participants understood technical terms related to RCT, but terms related to meta-analysis were more difficult to understand.

Addressing the Reproductive Health Needs of Women with Criminal Justice Histories

First Author: Tina Bui, MD Candidate; Megha Rammswamy PH.D, MPH

Introduction: Incarcerated women bear a disproportionate burden of sexual and reproductive health problems – higher rates of sexually transmitted infections (STI), unintended pregnancies, and cervical cancer – compared to women who don't have criminal justice histories. The objective of this presentation is to describe the factors associated with high sexual and reproductive health need, outline the few interventional strategies in place that address need, and offer recommendations for more comprehensive interventions at multiple levels – individual, institutional, and systemic.

Methods: We performed a targeted literature review on factors associated with incarcerated women's sexual and reproductive health risks, as well as strategies for intervention. We also summarized across findings from our own studies with women in Kansas City jails about women's STI, unintended pregnancy, and cervical cancer risks.

Results: Women, who generally have short but frequent stints in correctional facilities, are ambivalent about pregnancy prevention, tend to use the least effective prevention practices in the community, but accept the offer of more effective methods of contraception if offered to them in a timely and accessible manner. In their everyday lives, women with criminal justice histories also face real and tangible barriers to sexual and reproductive health success – homelessness, drug use, competing health problems, lack of health insurance, and limited transportation, for example. Nevertheless, incarceration provides a unique setting to deliver important reproductive health information and services.

Conclusion: Incarcerated women's sexual and reproductive health needs require a multi-faceted approach to their beliefs about prevention – an approach that is trauma-informed, oriented toward seamless and effective clinical practice, and gives women tools to navigate the disadvantages they face as they transition from correctional facilities to communities.

Chapter Winning Abstract

Emily Knittle, Ryan Eid, Benjamin Belknap, Mary Carter MD, PhD

Background: The Mufindi district in Tanzania's Southern Highlands suffers an HIV prevalence of 1 in 3, compared to 1 in 12 for the rest of Tanzania, and 1 in 300 for the US. In 2007 Foxes' Community and Wildlife Conservatory Trust (FCWCT) partnered with local leaders to establish a care and treatment center (CTC) and a home-based care (HBC) program, giving thousands of HIV patients access to antiretroviral (ARV) treatment. This study aims to evaluate HIV medication adherence among CTC patients.

Methods: This retrospective study was approved by the University of Louisville Institutional Review Board. In 2014, in an effort to evaluate the quality of their program by assessing medication adherence, HBC workers surveyed HIV+ patients about their social circumstances, patterns of medication adherence, and perceived barriers to taking medication. Surveys were created in conjunction with local leaders and deemed culturally sensitive by community leaders. HBC workers obtained verbal consent, administered the survey orally and documented participants' responses. ULSOM students Ryan Eid and Emily Knittle, after visiting Mufindi in 2014, were invited to retrospectively analyze the data. Data were analyzed using descriptive statistics, Pearson's rho and Chi Square, and are expressed as mean \pm SD. The null hypothesis was rejected for $p < 0.10$.

Results: ARV adherence was reported as 8.9 ± 1.0 on a 10-point Likert scale among a convenience sample of 21 women and 9 male participants. Demographics included: age 39.0 ± 9.9 years, 3.9 ± 2.8 years since diagnosis, 2.7 ± 1.8 years of treatment. Subjects who drank alcohol reported reduced ARV adherence ($p=0.005$) and were less likely to report having social support ($p=0.10$). Participants diagnosed with HIV since CTC establishment began ARV's closer to diagnosis than those diagnosed prior.

Conclusions: These results suggest that the CTC for HIV has been successful in initiating treatment in patients with HIV and that adherence is satisfactory. Alcohol use appears to be an ongoing barrier to HIV patient well-being in this population. Future studies are needed to evaluate the degree of alcohol use in this population and its effects on medication adherence.

Socio-demographic and Clinical Correlates of Micronutrient Intakes among Urban African Americans with Uncontrolled Hypertension

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Background: Dietary factors, influenced by social and cultural settings, may contribute to the high prevalence of uncontrolled hypertension in urban African Americans (AAs), and may raise their risk of poor health outcomes, including kidney disease.

Methods: In a randomized trial of 159 AAs in Baltimore with uncontrolled hypertension [Achieving Blood Pressure Control Together (ACT) study], we used the Block Fruit-Vegetable-Fiber Screener to estimate baseline daily intakes of vitamin C, magnesium, dietary fiber and potassium (estimation of sodium is not applicable for this screener). To determine the association between sociodemographic factors and micronutrient intakes, we used multivariable linear regression for continuous variables and logistic regression for categorical variables. Using logistic regression, we determined the association between micronutrient intakes and reduced kidney function [estimated glomerular filtration rate <60 ml/min per 1.73m² (eGFR<60)]. All analyses were adjusted for age and gender.

Results: Median intakes for magnesium, dietary fiber and potassium were lower than Institute of Medicine recommendations. Median intakes of vitamin C, magnesium and potassium were similar to estimations from the general U.S. population (National Health and Nutrition Examination Survey), whereas fiber intake was lower among ACT participants, by comparison. Sociodemographic factors statistically significantly associated with intakes (mg/d) of vitamin C, magnesium, dietary fiber and potassium (adjusted β coefficient [95% confidence interval]) were age ≥ 60 years (versus <60) ($\beta = -17.13$ [-30.04, -4.21]; $\beta = -46.24$ [-69.22, -23.27]; $\beta = -3808.04$ [-5329.06, -2287.02]; $\beta = -403.95$ [-630.22, -177.67]), male gender ($\beta = 32.31$ [18.28, 46.34]; $\beta = 102.12$ [77.46, 126.79]; $\beta = 5699.31$ [4083.51, 7315.11]; $\beta = 856.33$ [612.23, 1100.43]) and lower-than-median health numeracy scores ($\beta = -20.33$ [-32.70, -7.97]; $\beta = -35.69$ [-57.43, -13.95]; $\beta = -2296.72$ [-3722.47, -8709.72]; $\beta = -353.40$ [-568.53, -138.27]). Income, education, literacy, exercise, food insecurity, nor tobacco use were significantly associated with micronutrient intakes.

Lower (less than median) intakes of vitamin C (Odds Ratio (OR)=1.54 [0.61, 3.89]), magnesium (OR=1.65 [0.65, 4.21]), dietary fiber (OR=1.66 [0.65, 4.23]), and potassium (OR=1.59 [0.63, 4.05]) were associated with eGFR<60, but associations were not statistically significant following adjustment for age and gender.

Conclusions: AAs with uncontrolled hypertension may lack the recommended micronutrient intakes that could favorably influence their clinical outcomes. AA females, older adults and persons with low health numeracy may have particularly low intakes of beneficial micronutrients, suggesting a need for targeted interventions for these populations.

A Novel Compound, Membrane-Tethered E2, Selectively Activates the ER Rapid Signaling Pathway – Implications for Vascular Benefit

First Author: Seda Babroudi Additional authors: Qing Lu, Richard Karas

Introduction: Heart disease is the leading cause of death in both men and women in the United States despite disproportionately affecting men. In younger post-menopausal women, estrogen supplementation may decrease the risk of heart disease through its interaction with ER α and ER β in the vasculature. Upon binding ER, estrogen initiates two pathways: the rapid signaling pathway and the genomic signaling pathway, traditionally associated with dilatation of vessels and proliferation of endothelial cells, respectively. Estrogen supplementation, however, has been associated with an increased risk of breast and uterine cancer. Here we hypothesize that isolating the rapid pathway alone, using the novel compound membrane-tethered E2 (MT E2), is sufficient to mediate the beneficial vascular effects of estrogen without inducing the potential adverse effects.

Methods: Human endothelial somatic hybrid cells (EA.hy926) were treated with 100 nM MT E2 with the appropriate ligand controls. Activation of the rapid signaling pathway was measured by phosphorylation of specific downstream proteins (eNOS, AKT, and ERK). Activation of the genomic signaling pathway was measured by an ERE-luciferase assay. ER α was localized by immunocytochemistry, and proliferation and migration were measured by a cell viability and scratch-wound assay, respectively.

Results: Cells treated with MT E2 exhibited increased phosphorylation of eNOS, AKT, and ERK, suggesting that MT E2 activates the rapid signaling pathway. Cells treated with MT E2 did not, however, upregulate luciferase via an estrogen response element (ERE), suggesting that MT E2 is incapable of activating the genomic pathway. Unlike treatment with E2, MT E2 did not drive ER α to the nucleus, though it did induce proliferation and migration of vascular cells to an equal or greater extent than E2, suggesting that the rapid pathway is sufficient to induce vascular cell function.

Conclusions: In conclusion, we confirmed our hypothesis that the novel compound, MT E2, activates the ER rapid pathway without activating the genomic pathway, and by doing so, is sufficient to induce proliferation and migration of human endothelial cells to an equal or greater extent than conventional estrogen, supporting its potential vascular benefit in vivo.

Seeing Eye to Eye with Patients: Meeting Community Need for Medical Specialty Care

First Author: Elaine Downie Additional authors: Maximilian von Hohenberg, William Ladner, Andrew Harrison MD, Brian Sick MD

Introduction: Medical specialty care is often difficult to access for un- or underinsured patients. The Phillips Neighborhood Clinic (PNC) is a student run free clinic that provides primary and specialty medical care, via dedicated specialty clinic nights, to a largely underinsured neighborhood in Minneapolis. Prior to our project, specialty care offered at the PNC was limited to dermatology and foot care. In order to better serve community needs, we conducted a survey of PNC patients to assess the desire for a new area of specialty care and implemented a plan to provide that care.

Methods: PNC volunteers surveyed patients to assess interest in new specialty care. Survey questions were: "Are you interested in additional specialty nights at the PNC?" and "What specialty would you be interested in?" After community needs were assessed, the most requested specialty night was implemented. Patients are now surveyed at each specialty night to determine health insurance status, reason for visiting the clinic, and satisfaction with various aspects of their clinic experience (scale 1-5, with 1 being not satisfied and 5 being very satisfied).

Results: 100 patients were surveyed. The majority of the patients (84%) were in favor of having an additional specialty night at the PNC. The specialty most patients desired was ophthalmology (36%), followed by orthopedics (25%), gynecology (17%), psychiatry (12%) and other (10%). In response to the survey results, monthly ophthalmology specialty nights were implemented. Services provided include comprehensive eye exams, glaucoma screening, and refractions by University of Minnesota Department of Ophthalmology faculty and residents. Glasses are custom made and provided free of charge to patients by volunteer opticians via donations from Lens Crafters and Edina Eye Physicians and Surgeons. To date, there have been three ophthalmology nights. At these nights, 34 patients were seen and 17 were provided with glasses. One patient was diagnosed with a retinal hemorrhage and was urgently referred for continued evaluation and treatment. Of the patients that were seen, 74% were uninsured and 92% reported being very satisfied with all aspects of their clinic experience.

Conclusion: There is a large demand for medical specialty care for patients that are un- or underinsured. In the community served by our clinic, ophthalmology was the most requested specialty. Lack of health insurance is the largest barrier to eye care in resource poor communities. Having access to adequate eye care is important for multiple aspects of patient well-being as visual impairment predisposes patients to higher medical expense and further limits their access to healthcare. We have found a free way to provide our patients with this important service.

The role of the transcription factor Transforming Growth Interacting Factor in the pathogenesis of pancreatic ductal adenocarcinoma and diabetes

Subhi Talal Younes L. Ian Taylor Parash Parajuli Azeddine Atfi

Objectives: To examine the role of the transcription factor TGIF, a known downstream effector of the Kras signaling pathway and a part of the Wnt signaling network, in the pathogenesis and progression of pancreatic ductal adenocarcinoma, the most common form of pancreatic cancer.

Methods: Utilizing the LoxP-Cre system, we generated mice that selectively overexpress TGIF (Pdx.Cre+; LSL.TGIF) in all pancreatic progenitor cells, including islet, ductal, acinar, and centroacinar lineages. To further analyze the effects of TGIF on pancreatic carcinogenesis, TGIF overexpressing mice were crossed with mice expressing oncogenic Kras (Kras.G12D) in the pancreas.

Results: To date (7 months), mice overexpressing TGIF alone (TC mice) have not developed overt pancreatic ductal adenocarcinoma, but display diffusely abnormal tissue architecture of the pancreas and numerous pancreatic intraepithelial neoplasias, a pre-cancerous lesion of the pancreatic ducts. When combined with oncogenic Kras (TGIF+;Kras.G12D+), mice develop a rapidly growing, very aggressive pancreatic adenocarcinoma, to which they succumb within 3-4 weeks. Taken together, these results indicate that TGIF can function as a potent oncogene. Interestingly, TC mice were observed to develop severe hyperglycemia by age 1 month. Upon histologic examination, pancreatic islets were found to be hyperplastic with perturbed cellular architecture. Further characterization revealed an insulin-deficient state, despite high levels of insulin being present in the islets as determined by immunofluorescent staining. Furthermore, insulin- and glucagon-positive cells were found throughout the exocrine compartment.

These results aid in illuminating the mechanisms by which TGIF functions as an oncogene. First, we hypothesize that TGIF has a direct growth-promoting role as a downstream effector of the well-characterized Kras pathway. Second, through its ability to activate the Wnt canonical pathway, we postulate that TGIF could activate a stem cell-like program, promoting cellular de-differentiation and enhancing carcinogenic potential. Third, again through its interaction with the Wnt pathway, TGIF could activate the Hippo effector Yap1, further promoting cellular growth and division. Finally, by inhibiting insulin secretion with resultant hyperglycemia via a Wnt-dependent mechanism, TGIF overexpression serves to promote cancer formation and progression by enhancing the Warburg effect.

Conclusion: Pancreatic cancer is a very lethal malignancy due to its insidious onset and rapid growth and progression. By elucidating the molecular mechanisms underlying pancreatic carcinogenesis and progression, we aim to discover new opportunities for earlier diagnosis, better prognostic markers, and novel treatment options.

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An Automated Telemonitoring System for COPD Management

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INTRODUCTION: Chronic Obstructive Pulmonary Disorder (COPD) is an irreversible respiratory disease characterized by narrowing and inflammation of the airways. It affects over 15 million Americans and is now the third leading cause of death in the United States. Patients suffer from dyspnea, exercise intolerance, and frequent respiratory infections. 50-75% of all COPD-related medical costs are associated with COPD exacerbation episodes, and Medicare spends over \$475 million annually on COPD hospital-related readmissions. Regular monitoring of COPD patients through the use of a telemedicine system may facilitate early detection and management of these exacerbations. Previous investigators have demonstrated that COPD telehealth systems can be an effective means to monitor symptoms and reduce resource utilization. This pilot study demonstrates the development and proof-of-concept of a simple, automated system to intervene in patient care before dyspneic events developed into debilitating and costly exacerbations.

METHODS: We developed a generic system, Epharmix, that allows researchers to craft a condition-specific automated messaging sequence that utilizes existing telephone and SMS infrastructure. Messages for the Epharmix COPD system, EpxCOPD, were designed in collaboration with physicians, nurses, and medical students. The message sequence assesses daily breathing trends in COPD patients. We tested patient adherence and satisfaction with the system in an outpatient clinic of our affiliated hospital system. When a subject reported worsening dyspnea, an electronic alert was sent to their healthcare provider. The provider then contacted the patient to counsel them on how to return to a stable breathing state.

RESULTS: Over the course of the seven-month pilot, the system made 3,619 automated breathing assessments. The subjects' cumulative weekly response rate was 96% over the course of the study, and their normalized breathing scores consistently increased over time. The rate of reported dyspneic events fell by 64% over the seven months, possibly indicating patients were learning how to better manage their condition. Prompt reporting allowed the provider to remotely alter a dyspneic subject's plan of care without sending them to the emergency room. Feedback from a patient survey revealed high satisfaction with the service. 75% of respondents reported that they felt as if they were "in greater contact with their medical provider" by answering the automated phone calls. Economic sustainability of this system was demonstrated by performing a cost-benefit analysis using Chronic Care Management billing codes.

CONCLUSION: The results of this pilot study warrant further investigation of the EpxCOPD system for short and long-term COPD management. A 600 subject randomized-controlled trial to assess the impact of this system on hospitalizations, morbidity, and patient compliance began at Washington University in December 2015.

Regulation of Locomotor Activity to Amphetamine Injection by Acid-sensing Ion Channel 1a and 2 in Adult Mice

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Drug addiction remains remarkably difficult to treat. This is in part due to an incomplete understanding of the mechanisms underlying addiction. An emerging body of evidence demonstrates that ion channels in the brain's reward circuits play an important role in addictive pathophysiology. Acid sensing ion channels (ASIC) are densely expressed in the brain with ASIC1a and ASIC2 as the predominant subtypes. These channels are known for their vital role in regulating normal synaptic transmission. New evidence suggests ASIC1a promotes learning/memory and synaptic plasticity. ASIC2 functions are less well understood, but are involved with neurologic disorders and neuronal ischemia. Our study investigates the role of ASIC1a and ASIC2 in regulating behavioral responses to the stimulant amphetamine by utilizing ASIC1a and ASIC2 knockout mice. Acute amphetamine administration induced an attenuated locomotor response in ASIC1a knockout mice compared to wild type (WT). ASIC2 showed decreased responses on day 2 and 3 of administration compared to WT. In a chronic amphetamine administration model utilizing a two week withdrawal followed by a challenge dose, ASIC1a and ASIC2 showed no significant difference from WT locomotor responses. Our results provide further insight into the role of ASIC channels in the modulation of behavioral sensitivity of amphetamine and addiction. These ASIC subtypes are believed to play significant roles in regulating responses to amphetamine and the synaptic plasticity leading to addiction.

Restless Leg Syndrome and its Association with Iliofemoral Venous Disease

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Background: Restless leg syndrome (RLS) is one of the most common sleep disorders, affecting between 5% and 10% of the U.S. population.¹ However, it has an unclear etiology, and is often over-medicated without a resulting qualitative improvement in lifestyle. It has not been determined whether iliofemoral or ilio caval venous disease resulting from either thrombotic lesions or external compression, has any association with RLS.

Methods: A total of 510 patients treated for iliofemoral venous compression syndrome (IVCS) with angioplasty and stenting were documented to have concomitant RLS per NIH screening criteria,² prior to endovenous revascularization. 367 of the following patients were selected for retrospective research analysis based on pre-procedural selection criteria which included: IVCS with > 60% luminal stenosis, confirmed RLS > 1 year with or without current treatment, diminished quality of life, and clinical signs and symptoms of chronic venous disease. Patients with Diabetes, End stage renal disease, current pregnancy, and Rheumatic disease were excluded from this study. Patients with thrombotic lesions of the iliofemoral veins were also excluded. Following revascularization, patients were followed at 6 weeks, 3 months, and 6 months with doppler evaluation and asked to rate the severity of their RLS using a scale developed by the International Restless Leg Syndrome study group.³

Results: Of the 367 patients studied, 52% of patients had improvement of their RLS symptoms at 3 months, 90% reported significant relief with cessation of medication(s) within 6 months and 11% did not have any statistically significant improvement by 6 months ($p < 0.001$).

Conclusion: This study demonstrates a strong relationship between deep vein obstruction and RLS. It is suspected that a large population suffers from iliofemoral venous disease, and including this subset of patients in the differential diagnosis for RLS can allow for earlier treatment of IVCS and prevention of RLS.

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Reducing Overutilization of Cardiac Telemetry through Targeted Education

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Introduction: Cardiac telemetry allows healthcare providers to monitor for dangerous arrhythmias. The American Heart Association (AHA) has published indications to determine which patients benefit from telemetry. Patients without an indication are unlikely to benefit from telemetry while incurring excess cost. The Society of Hospital Medicine (SHM) has identified this issue as a focus through the Choosing Wisely campaign, and recommends that telemetry be avoided in patients without a protocol for discontinuation. The University of New Mexico does not require an indication to initiate telemetry, lacks a protocol for discontinuation, and has a high percentage of patients on telemetry without an order.

Methods: We collected baseline data, over two days in February and March 2015, which showed a significant number of patients on telemetry without an order. Using this data, we presented this project in a best practices format to the faculty in the Division of Hospital Medicine and some nursing leadership. We recruited a nurse manager to act as a champion of the project. With nursing input, we developed a poster including the indications for telemetry and problems with its overuse. We placed these posters at nursing stations on medicine floors at our facility. Data collection continued at 2 week intervals to assess pre-determined statistics on telemetry use and order status.

Results: Initial data covered 72 patients. We found that 39 (54%) were on telemetry and 8 (21%) did not have an order. After presentation at Hospital Medicine Best Practices and recruitment of a nursing champion, another 120 patients were reviewed over four days. Of these post intervention patients, 67 (56%) were on telemetry and 7 (11%) did not have an order. The results following poster distribution are pending.

Conclusion: Our facility has a large subset of patients on telemetry without an order and strategies to address this issue have not been reported extensively in the literature. Our educational interventions have decreased the use of telemetry on patients without an order by 50% over four months. Telemetry costs our facility about \$53 per day, and this decrease use amounts to significant savings, while improving the patient experience and decreasing the risk of further unnecessary diagnostic testing. Although our educational interventions have had an impact on limiting overutilization of telemetry, more interventions are necessary to achieve sustained change. Next-step interventions include changing the ordering system to require that an indication be specified before initiating monitoring and potentially restricting access to telemetry equipment without an appropriate order. Although these interventions may ultimately be needed in order to reduce the overutilization of telemetry, the educational projects explored in this study form a framework for change by prompting staff to consider indications prior to initiating telemetry.

AN INTERVENTION IN THE ASSESSMENT OF THROMBOPHILIA DECREASES INAPPROPRIATE TESTING

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Introduction Thrombophilias occur as a result of a variety of inherited and acquired abnormalities. However, the risk for developing a venous thromboembolism (VTE) is not fully dependent on having an acquired or genetic abnormality. The question then remains, after a VTE, when is testing indicated for a potential thrombophilic predisposition? The main reasons to consider testing are to: a) Look for an underlying cause of an unprovoked VTE and b) assess the probability of a repeat event thereby guiding duration of anticoagulation therapy. In order 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 hypothesized that the HCPAN was being utilized outside of guideline-directed diagnostic utility. After our initial analysis of the data, we concluded that the majority of tests were being ordered outside of the recommended guideline. At this time, we implemented an intervention, eliminating the order set from the routine laboratory orders for subspecialties that ordered the most tests.

Methods: An intervention was implemented to decrease the number of routinely “over-ordered” HCPAN tests per international guidelines. The HCPAN was removed from the general order sets in place of specified order sets (e.g. APLA panel) for medical disciplines with statistically higher usage (e.g. Rheumatology). We compared the number of panels ordered from 9/13-3/14 to those ordered from 9/14-3/15. This included adult inpatient and outpatient HCPAN tests. We conducted a manual chart review, 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: While preliminary data indicate minimal correlation with ordering the panel and the status of the thrombophilic event, we did decrease the number of panels ordered by approximately 57%. With a cost analysis, we concluded that the intervention saved the hospital \$49,023. The results also indicated that although the overall number of panels ordered decreased, approximately 93% of those still being ordered were classified as ‘inappropriate’ as defined by our criteria.

Conclusion: The data indicates that most HCPAN tests are ordered outside of recommended guidelines, including being ordered for a provoked VTE, in the presence of anticoagulant, or during an active VTE. Furthermore, our results indicate that the HCPANs are ordered as a whole when only a small number of tests were indicated. Although removal of the panel from the general routine order sets significantly decreased the number of panels being ordered, many of those being ordered are still not within guidelines, indicating a need for further quality improvement-based educational interventions.

Bivalirudin vs Unfractionated Heparin After Transradial and Transfemoral Percutaneous Coronary Intervention in Patients With Stable Angina: A Randomized Controlled Trial (STATUS-PCI).

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Background: Both unfractionated heparin (UFH) and bivalirudin are currently used in patients undergoing percutaneous coronary intervention (PCI). There is limited data comparing UFH with bivalirudin in patients with stable angina undergoing PCI via the femoral or radial artery.

Aim: To examine the outcomes associated with radial vs. femoral access in patients with stable angina undergoing PCI treated with either UFH or bivalirudin.

Methods: STATUS-PCI is a prospective, investigator initiated, single-center, single-blinded, randomized 1:1 trial comparing UFH with bivalirudin in patients with stable angina or silent ischemia undergoing PCI. The primary endpoint of the study was all major and minor bleeding (REPLACE-2 trial definition) during the index hospitalization and up to 30-days post index-procedure. Secondary endpoints included major adverse cardiac and cerebrovascular events (MACCE)(all-cause mortality, myocardial infarction, ischemia driven target vessel revascularization, and cerebral vascular accident) and net adverse cardiac events (NACE)(composite of MACCE and major bleeding events until 30 days post index-procedure).

Results: A total of 260 patients were randomized to UFH (n=123) or bivalirudin (n=137). There were no significant differences in baseline clinical characteristics between the two groups. Radial access was used in 67 patients and femoral in 193 patients. At 30 days follow-up there was no difference in the primary endpoint of the study, all major and minor bleeding which occurred in 7.3% of patients randomized to UFH and 10.9% of patients randomized to bivalirudin (p=0.31). Major bleeding rates were 1.6% and 2.2%, p=0.74 respectively. Bivalirudin compared with UFH resulted in increased MACCE rates (0% vs. 3.6%, p=0.03). NACE rates were also higher in the bivalirudin arm but did not reach statistical significance (1.6% vs. 5.8%, p=0.08). Death and stent thrombosis rates were low and similar in both groups. No significant difference was seen in the primary endpoint in patients that had femoral access or radial access (10.4% vs. 6.0%, p=0.29) or MACCE rates (2.1% vs. 1.5%, p=0.77). Major bleeding rates (2.1% vs. 1.5%, p=0.77) and NACE rates (4.7% vs. 1.5%, p=0.25) were also similar in both groups. Overall bleeding rates were also identical in patients treated with UFH or bivalirudin transfemoral (10.9% vs. 10.0%, p=0.83) or transradial (5.7% vs. 6.3%, p=0.83).

Conclusions: Among patients with stable ischemic heart disease undergoing PCI on dual anti-platelet therapy, there was no significant difference between UFH and bivalirudin with respect to all major and minor bleeding events, or NACE at 30 days post-procedure. However, there was a significant increase in MACCE rates in patients treated with bivalirudin. Radial access was associated with a numerically lower rate of bleeding complications when compared with femoral access, but did not reach statistical significance.

RACING AGAINST THE CLOCK – INTERNAL MEDICINE RESIDENTS' USE OF ELECTRONIC MEDICAL RECORDS

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Introduction: For the past 20 years, increasing amounts of time were spent on clinical documentation. The implementation of Electronic Health Records (EHR) resulted in both physicians and patients complaining that physicians spent more time on computerized patient records than at the bedside. This study provides objective and longitudinal analysis of the time spent using EHR by Internal Medicine (IM) residents over the span of an academic year.

Methods: Active EHR usage data was collected from the EHR audit logs for IM residents from July of 2014 thru June of 2015. Active EHR use was defined as more than 3 mouse clicks, 1,700 mousemiles or 15 keystrokes per minute. EHR usage activities were divided into four sub-categories: Chart Review, Placing Orders, Documentation, and Other Activities. Electronic patient encounter (EPE) was defined as the total active EHR usage time on the same patient record within a single day. A total of 109 residents (41 PGY1, 31 PGY2, and 37 PGY3) were identified and included in the study.

Results: During the academic year, 109 residents accumulated 112,705 hours of active EHR use on 165,293 EPEs. An average resident spent most time per EPE in July and least amount of time in June (47 min vs. 33 min, $p < 0.001$). Statistically significant reductions in time were also noted in three sub-categories of EPE: Chart Review (17 min vs. 12 min), Placing Orders (9 min vs. 6 min), and Other Activities (10min vs. 6 min, all $p < 0.001$). In addition, a modest reduction was seen in Documentation (11min vs. 9 min, $p = 0.2$). In July, each resident spent an average of 26 hours on clinical documentation in an 80-hour workweek. In June 2015, this amount was effectively reduced to 18 hours per workweek (a 31% reduction).

Conclusion: Resident physicians spent a significant amount of their duty hours actively using EHR. Although reducing clinical documentation time due to increased proficiency and familiarity with EHR is observed. Further curtailing of time spent documenting on a computer is needed in order to optimize a physician's presence at the bedside.

Risk factors and strategies to improve survival of cardiac arrest patients in a community hospital in Brooklyn

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Introduction: Each year there are approximately 200,000 in-hospital cardiac arrests in U.S hospitals and this rate may be increasing. This is important for understanding the burden of in-hospital cardiac arrest and developing strategies to improve care for hospitalized patients. In our retrospective pilot study, our main goal is to find the most common associated factors in cardiac arrest in this community to prevent avoidable cardiac arrest, in order to reduce the unnecessary utilization of resources.

Methods: All data of in-hospital cardiac arrest events which happened from February to August 2015 at Kingsbrook Jewish Medical Center were collected. . Patient demographics, co-morbidities, routine lab testing (arterial blood gases, comprehensive metabolic panel, lactate) prior to cardiac arrest, initial EKG rhythms and cause of death were collected. Patients designated as Do Not Resuscitate (DNR) and those that had cardiac arrest on arrival at the emergency department were excluded

Results: There were 3516 adult admission from February to August 2015 and a total of 175 deaths. The cardiac arrest team was activated 63 times: 61 were for primary in-hospital cardiac arrest, 9 cases were excluded due to incomplete data. Among the rest (52), the 24 hr post cardiac arrest survival rate was 19.2% (10 out of 52), and survival rate until hospital discharge is 3.8 % (2 out of 52). The mean age of in-hospital cardiac arrest was 70. We observed that the majority of cardiac arrest events were associated with septic shock, most commonly associated with carbapenemase producing type of klebsiella pneumoniae (KPC) in this community (3 out of 7 septic shock patients). Hypoxemia with a normal PH (7.35 to 7.45) , NSTEMI and electrolyte abnormalities (hypokalemia and hyperkalemia) are the second, third and fourth most common associated factors, respectively. The most common initial rhythm prior to cardiac arrest was asystole.

Conclusion: Based on our pilot study, we found that septic shock associated with carbapenemase producer KPC, acid-base disturbance and NSTEMI are the most common risk factors associated with cardiac arrest in this inner-city Brooklyn community. Further prospective study is necessary in order to deduce predictors and strategies to prevent avoidable cardiac arrests.

Admission Characteristics in Uncomplicated Lower Extremity Cellulitis: Establishing the Need for Admission Clinical Decision Rules

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Introduction: Despite the prevalence of cellulitis seen in the emergency department, there are no validated clinical decision rules to support which patients require admission for lower limb cellulitis (LLC), as there are for patients with community acquired pneumonia (CAP). Development of a clinical decision rule for LLC may prevent unnecessary hospital admissions for uncomplicated LLC, similar to what has been shown for patients with CAP. The objective of the study was to describe demographics, co-morbidities, admission vitals, and laboratory markers of infection among patients hospitalized for LLC as compared to those for CAP.

Methods: A cross sectional retrospective nested case control study was performed at 3 networked hospitals in the North Shore LIJ Health System in order to summarize patient characteristics. Univariate and multivariate models were created to estimate likelihood of independent variables being associated with LLC admission, compared to CAP admission. We included patients over 18 years of age identified by a primary admitting diagnosis of LLC without abscess between 2009 and 2014. The comparison cohort was established by identifying subjects over 18 years of age with a primary admitting diagnosis of CAP during the same period.

Results: There were 4244 admissions for LLC and 5544 for CAP over the five year study period. The median age for patients with LLC was 65.8 vs. 77.2 for CAP. Diabetes (OR: 1.41, CI 1.27-1.56) and obesity (OR: 2.28, CI 2.06-2.52) were more common among patients with LLC. Smoking (OR: 0.89, CI 0.81-0.98) was slightly less common in LLC. No significant difference was found in the frequency of hypertension (OR: 1.09, CI 1.00-1.18). Patients with LLC were significantly less likely to have fever [OR 0.36, CI 0.28-0.46], tachycardia [OR 0.49, CI 0.41-0.58], or hypotension [OR 0.50, CI 0.39-0.64] compared to patients with CAP, and were also significantly less likely to be admitted with leukocytosis [OR 0.75, CI 0.66-0.85] or neutrophilia [OR 0.50, CI 0.44-0.57].

Conclusions: Patients with LLC were more likely to be obese and have diabetes, but less likely to smoke, have vital sign abnormalities, or laboratory markers of infection compared to patients with CAP. Whether these findings are important in clinical decision making regarding the need for hospitalization can only be determined with further prospective studies. The lack of validated clinical decision making rules could potentially result in a higher admission rate than necessary.

Uncomplicated Lower Limb Cellulitis and Clinical Risk Factors that May Affect Length of Stay

G Lin, J Lavian, C Sison, M Oppenheim, B Koo, A Garg

Background: Despite the significant costs associated with lower limb cellulitis (LLC) admissions, there are no validated clinical decision rules to stratify patients at risk for a prolonged hospital stay, who may require escalated inpatient management.

Objectives: To describe demographics, co-morbidities, admission vitals, and laboratory markers of infection among LLC patients with prolonged hospital stay >5 days.

Methods: A retrospective case control study was performed at 3 networked hospitals in the North Shore LIJ Health System. Univariate and multivariate models were created in order to estimate the likelihood of variables associated with prolonged length of stay (LOS) >5 days. Patients 18 years old or older with a primary admitting diagnosis of LLC without complications between 2009 and 2014 were included in the study.

Results: There were 4209 admissions for LLC with 1662 having a LOS >5 days (39.5%). The median age for LOS >5 days was 70.1 vs. 63 for LOS <5 days. Age >50 years old [OR:2.21, CI:1.87-2.60], hypertension [OR:1.19, CI:1.04-1.35], diabetes mellitus [OR:1.34, CI:1.15-1.56], tachycardia [OR:1.57, CI:1.28-1.92], hypotension [OR:1.69, CI:1.25-2.27], WBC >10.5 [OR:1.60, CI:1.41-1.82], neutrophil percentage >77 [OR:1.97, CI:1.72-2.26], bicarbonate <22 [OR:1.73, CI:1.42-2.12], creatinine >1.3 [OR:2.15, CI:1.87-2.47] were associated with a prolonged hospital stay.

Conclusions: Patients with age >50, hypertension, diabetes mellitus, vital sign abnormalities, and laboratory markers of infection were more likely to have a LOS >5 days. Patients with multiple risk factors for LOS >5 days may merit escalated inpatient management including Infectious Disease or Dermatology consultation to prevent a prolonged hospital course. Further prospective studies are needed to validate these risk factors and determine risk-stratification rules for LLC.

Sources of non-emergent low acuity ED use: Are our colleagues to blame?

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Introduction: Emergency Department (ED) crowding threatens patient safety and has been associated with delays in treatment, decreased quality of care and increased mortality. A major modifiable factor that produces ED crowding is non-emergency provider directed referrals. In this patient survey, we identify factors responsible for low acuity patients seeking ED care.

Methods: We surveyed consecutive patients with an Emergency Severity Index (ESI) of 3, 4, or 5 at a single urban 525 bed tertiary care hospital between the hours of 8 a.m. and 12 am from February 8, 2014 to March 2, 2014. This timeframe was chosen to meet our initial target of 1,000 surveys, which we believed would yield a sufficient number of patients who had gone to our ED because they could not arrange alternatives. Research volunteers did not approach psychiatric or isolation patients for safety reasons. Patients brought in by ambulance or whose acuity was upgraded were also excluded. We analyzed the subset of patients who approached the ED on weekdays between 8 AM and 3 PM separately as these patients may have had alternatives to the ED during those hours. The institutional IRB considered our survey process exempt from full review.

Results: 1,108 of the 1,648 approached patients consented and completed the survey adequately. 579 (52%) patients spoke with a medical provider prior to the ED visit, 405 (70%) of whom were directed to the ED. Patients were able to identify that other settings would have been appropriate alternatives to the ED, with 654 (59%) patients of the total 1,108 indicating that they would have accepted a clinic appointment in lieu of the ED. Of the 654 patients who would have accepted a clinic visit, 307 (47%) indicated a preference for a specialty (non-primary care) clinic. We found little difference in survey response patterns between those patients who presented between 8AM and 3PM and those who presented at other times.

Conclusion: The majority of our low acuity ED patients claim they would have been satisfied with timely ambulatory care, yet many were advised to come to the ED. These results suggest that averting avoidable ED use requires that community physicians be trained to refer patients to alternative sources and that the number of available alternatives be increased. This lack of education along with the failure to develop alternatives may explain why increased insurance coverage from ACA or Medicaid programs has been reported to be associated with higher ED utilization.

Metformin Reduces Mitochondrial Degradation in Doxorubicin Treated Cardiac Myoblasts

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Background: Doxorubicin (DOX) is among the most effective and widely used antineoplastic agents for the treatment of a wide variety of cancers including both solid tumors and leukemias. However, its usefulness is compromised by its cardiotoxicity. It has been known that Metformin (MET) can rescue myocardium from DOX-induced damage. Given its cardioprotective properties, MET may be used in DOX-containing chemotherapy to reduce its cardiotoxic effect. Preliminary studies have demonstrated that DOX induces excessive mitochondrial fragmentation and degradation.

Objective: We tested the hypothesis that MET protects against DOX-induced cardiomyocyte injury by inhibiting excessive degradation of mitochondria through the autophagy-lysosome pathway (mitophagy).

Methods: H9C2 cardiac myoblasts were cultured in 10% fetal bovine serum containing medium. Cells were incubated with DOX (1 μ M) for 16hrs. MET (1 mM, 3 mM, and 5 mM) were added 24 hrs prior to DOX treatment. Propidium Iodide (PI) staining was used to determine DOX-induced cardiomyocyte death. Apoptotic cell death was determined by the cleavage of PARP in Western blot analysis. To evaluate the level of mitophagy, an adenovirus encoding mitophagy reporter (AdmtRosella) were infected in cells 24hrs before treatments. MtRosella is composed of a mitochondrial targeting sequence and a RFP-GFP fusion protein. Using confocal microscopy the fragmented mitochondria degraded in the lysosome were detected as red puncta where the pH sensitive GFP is quenched, while the rod-shaped mitochondria were detected as yellow in the green/red merged image. The numbers of red puncta were counted to evaluate the level of mitophagy.

Results: DOX increased the number of PI positive cells and the level of PARP cleavage, which were attenuated by Metformin. In the mitophagy reporter assay, DOX increased the number of red puncta, the signature of mitophagy, while it was reversed by MET at the dose providing protection against DOX.

Conclusion: Metformin protects against Doxorubicin-induced cardiotoxicity. The inhibition of mitophagy by Metformin may explain the mechanism behind cardioprotection

Screening for Obstructive Sleep Apnea in Adult Psychiatry Clinic

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The rate of undiagnosed obstructive sleep apnea (OSA) is very high in the general population, and there is significant comorbidity between OSA and mood disorders. To further complicate this issue, many OSA symptoms, such as daytime sleepiness, are difficult to differentiate from symptoms of mood disorders. In this study, we screened patients with mood disorder symptoms that might also represent undiagnosed OSA, to investigate whether they had been identified and referred to a sleep clinic for further evaluation. We also examined the frequency at which patients at intermediate to high risk for OSA were being prescribed sedatives to manage their mood disorder symptoms.

138 patients at the outpatient Psychiatry clinic at Albany Medical Center, were screened for OSA symptoms and risk factors. Participant STOP-BANG scores were used to identify those at high risk for developing OSA. Electronic medical records were reviewed to identify the medications prescribed to these patients at the clinic.

115 patients had complete data for the STOP-BANG questionnaire. Within this group, 29 (25%) were found to be at high risk for OSA, and 32 (28%) were found to be at intermediate risk for OSA. Of these patients (both intermediate- and high-risk), 30 (50%) had been referred to a sleep clinic. However, only 1 of these patients had been referred by a provider at the Albany Medical Center Psychiatry clinic. 44% of the patients in the intermediate-to high-risk group were being prescribed sedatives by their mental health provider.

In conclusion, OSA screening can be done very easily; however, in our sample, the rate of referral to a sleep clinic for further evaluation was very poor. In fact, most patients who met elevated risk criteria had not been advised to follow up with a sleep specialist. We also found that in our sample, nearly half of the patients with elevated risk criteria were being prescribed sedatives by their mental health providers. Prescribing sedatives to patients at intermediate or high risk for OSA without full evaluation is not recommended, as this practice may actually worsen patients' symptoms. This study highlights the importance of raising provider awareness of OSA within psychiatric populations, and educating them about appropriate referral sources for further evaluation.

Analyzing Tumor Response to a Ketogenic Diet and Concurrent Autophagy Inhibition In Vivo

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Introduction: Tumors are unable to grow without a nascent blood supply. As they outgrow their supply, ischemic stress occurs. Autophagy is an organized degradation of intracellular components and is critical for nutrient scavenging under stress. Autophagy blockers have been shown to decrease the cell's ability to overcome ischemic micro-environments.

When glucose is low, mitochondria utilize amino acids as an energy source. Contrarily, many cancer cell types rely predominantly on glucose-dependent anaerobic glycolysis. A low-glucose diet has been shown to significantly decrease tumor growth.

We propose that combining this diet with autophagy inhibition will have a synergistic effect on tumor regression. This experiment investigates the effects of ketogenic diet combined with Chloroquine (CQ), an autophagy inhibitor, on tumor growth in mice.

Methods: In this experiment, 30 mice were injected subcutaneously with oncogenic Bax/Bak knockout cells. The mice were divided into 6 treatment groups with 5 mice per group. Each treatment group was fed one of: Western, high-fat or high-protein ketogenic diet in the presence or absence of CQ.

The mice were monitored daily for tumor progression over 58 days by measuring tumor length and width to calculate volume. Tumor volume was compared using t-test and ANOVA. Tumors were excised and stained with H&E and mitochondrial markers (VDAC & ATPB) for immunohistochemical analysis. Tumor lysates were generated for Western blot analysis of mitochondrial protein.

Results: The growth of CQ tumors, using Western diet, was 43% relative to the control ($p = 0.02$). The high-protein and high-fat ketogenic diet displayed tumor growth at 17.7% ($p = 0.016$) and 16.4% ($p = 0.0035$) relative to control. The combined high-protein and CQ treatment group grew 21.6% ($p = 0.0023$) relative to control. The combined high-fat and CQ treatment group grew 20.27% ($p = 0.0027$) relative to control.

Immunohistochemistry demonstrated mitochondrial presence was notably decreased in the groups without CQ. Western blot analysis confirmed a decreased mitochondrial presence in the groups that did not receive CQ treatment. H & E stain displayed increased necrosis in CQ treated tumors compared to controls.

Conclusion: The effects of the ketogenic diet and CQ decreased tumor growth. Interestingly, combined ketogenic and CQ treatment groups grew at a greater rate than either treatment alone. When a cancer cell is unable to survive off of nutrients from the blood supply, such as when fed a ketogenic diet, it relies on autophagy for nutrient scavenging. Adding CQ blocks the cancer cell's ability to use autophagy, however, it may force the cell to divert to aerobic metabolism in order to maintain survival.

Tissue Transglutaminase Mediates Myofibroblast Differentiation in Primary Human Lung Fibroblasts

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Background: Idiopathic Pulmonary Fibrosis (IPF) is a progressive, fibrotic lung disease of unknown etiology that affects more than 200,000 people in the United States. There are few effective therapies and the median survival from the time of diagnosis is 2.9 years. The pathological hallmark of IPF is the transformation of lung fibroblasts into myofibroblasts, which accumulate in clusters called fibroblastic foci. Myofibroblasts produce excess collagen, α -smooth muscle actin (α SMA,) calponin and extracellular matrix proteins in the lung interstitium, eventually resulting in scar formation and compromise of lung function. One key cytokine responsible for myofibroblast differentiation is transforming growth factor (TGF) β . Our lab has shown that in addition to inducing myofibroblast differentiation, TGF β also induces the expression of lactate dehydrogenase-A (LDHA) in primary human lung fibroblasts¹. Lactic acid and LDHA are both elevated in the lungs of patients with IPF suggesting that the LDH enzyme may be an important part of the pathogenesis of IPF¹. Another potentially important protein involved in tissue fibrosis and progression to IPF is tissue transglutaminase (TG2.) Our lab has shown that TG2 expression is increased in the lungs of patients with IPF, and that TG2 knockout mice are largely protected from developing pulmonary fibrosis when exposed to bleomycin, a pro-fibrotic chemotherapeutic agent². While both TG2 and LDHA are likely important proteins involved in the progression of IPF, there is no known link between the two enzymes in lung fibrosis. Here, we hypothesize that intracellular TG2 regulates LDHA expression in human lung fibroblasts and that inhibition of TG2 will inhibit myofibroblast differentiation.

Methods: To examine the effects of TG2 inhibition on LDHA expression in human lung fibroblasts, Short Hairpin (Sh) RNA lentiviral vectors targeting TG2 and a scrambled Sh-RNA were used to knockdown TG2 expression. Similarly, a lentivirus vector was used to overexpress wild type TG2 and W241A, transamidation deficient mutant TG2. These cells were cultured and treated with TGF β . Cell lysates were harvested 72 hours post-treatment. Protein expression levels of LDH5, α SMA, calponin, TG2 and GAPDH were measured by Western blot.

Results: In normal lung fibroblasts, TGF β induced expression of LDHA, α SMA and TG2. Overexpression of LDHA in HLFs resulted in increased myofibroblast differentiation (increased α SMA expression.) Our results show that TG2 inhibition decreased the expression of LDHA, calponin, α SMA and TGF β induced α SMA expression compared to controls. Wild type TG2 overexpression increased expression of LDHA, calponin and α SMA. However, overexpression of the the transamidation deficient mutant of TG2, W241A, did not increase expression of calponin or α SMA.

Conclusion: These data suggest that the TG2 may induce expression of LDHA in human lung fibroblasts, which may be an important driver of the excess lactic acid found in the lung tissue of patients with IPF. The interplay between these two enzymes could be crucial for the progression to pulmonary fibrosis. In addition, these data suggest that transamidation activity of TG2 is necessary for promoting myofibroblast differentiation in the lung.

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2. Olsen KC et al (2011). *Am J Respir Crit Care Med*, 184:699-707.

Mitophagy Contributes to Doxorubicin-Induced Cardiomyocyte Death

First Author: Ashley Weiner

Doxorubicin (DOX), one of the most commonly used antineoplastic agents, is effective against many cancers, but limited by its toxicities on non-cancerous cells, especially cardiomyocytes. Although some strategies have been attempted, development of a specific therapy targeting DOX-induced heart failure has not yet been created, largely because the mechanism remains poorly understood. DOX sets off a cellular cascade leading to mitochondrial disruption, with cell death being the ultimate event. Since mitochondrial density is up to 35% in cardiomyocytes, DOX-induced mitochondrial malfunction can cause a serious shortage of energy supply. In this study, we investigated whether DOX treatment results in excessive elimination of mitochondria through the autophagy-lysosome pathway known as mitophagy, and if this leads to an increase in cardiomyocyte death. Mitochondrial morphology and the levels of mitophagy in DOX-treated H9c2 cardiac myoblasts were examined with adenovirus-encoded mtRosella, a mitochondrial-targeted pH sensitive dual fluorescent fusion protein. Confocal imaging analyses show that DOX enhanced mitochondrial fragmentation and increased mitophagy. To determine the underlying mechanism that mediated DOX-induced mitophagy, we examined the expression levels of several proteins that regulate mitophagy. The serine/threonine protein kinase PINK1 and the E3 ubiquitin ligase Parkin comprise a well-established pathway involved in the activation of mitophagy. The protein levels and mitochondrial translocation of Parkin and PINK1 were all increased at 2 hours after DOX treatment, but only the effects on PINK1 were sustained at 24 hours. Parkin levels were actually reduced at this time point. These results suggest that the PINK1/Parkin pathway may contribute to DOX-induced mitophagy and cell death. Indeed, overexpression of Parkin via adenovirus-mediated gene transfer accelerated DOX-induced mitochondrial morphology changes and induced mitophagy, which was associated with exaggerated cell death as indicated by propidium iodide (PI)-uptake and cellular levels of cleaved caspase-3 and cleaved Poly ADP ribose polymerase. Conversely, Parkin knockdown by siRNA inhibited DOX-induced mitophagy and reduced apoptotic marker levels and PI-uptake. These results suggest that DOX-induced mitochondrial fission and mitophagy are detrimental to cardiac cells. Strategies that limit mitochondrial degradation through PINK1/Parkin mediated mitophagy may help reduce DOX cardiotoxicity.

Patient Expectations and Satisfaction in an Orthopedic Clinic

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Upon implementation of the Affordable Care Act, doctors will be evaluated and paid based on the quality of care they provide instead of quantity. One measure of quality of care is based on patient satisfaction through the Consumer Assessment of Healthcare Providers and Systems Survey (CAHPS). We wished to evaluate the role that patient expectation plays regarding patient satisfaction in orthopedic specialty clinics. While studies have explored expectations in primary care and urgent care settings, this study is novel in investigating the role of expectations in a joint replacement and sports medicine clinic. Patients (n = 104) were given two surveys, a pre-visit questionnaire and a post-visit questionnaire with options based on the CAHPS survey. Patients were asked to select common services that they expected from their appointments, rate their doctors on Likert scales, and report their appointment outcomes. Despite leaving with unmet expectations (recommendations for surgery or prescriptions for narcotics), patients still gave their doctors high satisfaction rates (9.22/10 and 9.20/10 respectively). Furthermore, patients who only got “advice and education,” gave their doctors an average rating of 9.3/10. Thus, this study reports that regardless of meeting expectations, if a physician treats patients well and provides patients with appropriate care, patients will still rate him or her highly.

**Note:* Project is ongoing. Updates to abstract will occur as more data is collected.

Upon implementation of the Affordable Care Act, doctors and hospitals will be evaluated based on the quality of care they provide, linking doctors’ payments through Medicare to quality of care as opposed to quantity. One measure of quality of care will be based on patient satisfaction through a satisfaction survey called Consumer Assessment of Healthcare Providers and Systems Survey (CAHPS). Due to contradictory evidence in the literature, we wished to evaluate the role that patient expectation plays regarding patient satisfaction in a joint specialty clinic. While there have been a number of studies regarding expectations in a primary care and urgent care setting, this study is novel in investigating the role of expectations in a joint specialty clinic. Patients (n = 71) were given two surveys, a pre-visit questionnaire and a post-visit questionnaire with options based on the CAHPS survey. Patients were asked to select common orthopedic services that they expected from their appointments, rated their doctors on Likert scales, and reported the outcomes of their appointment. Despite having the unmet expectations of receiving recommendations for surgery and prescriptions for narcotics, patients still gave their doctors high satisfaction rates (9.3/10 and 9.5/10 respectively). Furthermore, patients who only got “advice and education,” gave their doctors an average rating of 9.3/10. Thus, this study reports that regardless of patient expectations and if those expectations are met, if a physician treats patients well and provides them with appropriate medical care, patients will still rate him or her highly.

A Pilot Program in Teaching Cost and Value in Morning Reports.

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Background: The lack of formal training on cost awareness in the traditional graduate medical curriculum fosters an environment for potentially wasteful spending habits that contribute to the unsustainable cost for healthcare in the United States. Simple additions to the current curriculum can increase the discussion and adoption of high value care (HVC) into every day practices.

Objective: This is a pilot study to test the educational quality of integrating an interactive HVC lecture and an innovative computer assessment tool to the current graduate medical education curriculum in the Department of Pediatrics residency program at UNC Hospitals.

Methods: The HVC lectures are a clinical didactic case that are delivered once a month from October 2015 to October 2016 to all pediatric faculty, residents, and medical students at UNC Hospitals. Each clinical case is divided into three breaks where participants use a wireless device to complete a multiple-choice survey of the tests and treatments they would like to order at the time. Prices for tests and treatments are received from McClendon Labs at UNC Hospitals or the Healthcare Bluebook. Each case concludes with the patients' diagnosis and a review of the diagnostic algorithm with prices of each test recommended for the case. Data analysis is performed in R studio. The recommended charged sum will be compared with each individual survey response. Following the lecture, a report on each individual's response is emailed to all participants to allow them review their responses and learn from their behaviors.

Results: Of the approximately 70 residents and 40 faculty members in the department of Pediatrics, 52 residents and 3 attending physicians have participated in the first lectures. The lecture series with the electronic feedback system have been met with support from all participating residents and physicians. Preliminary results show varying levels of knowledge on established diagnostic algorithms for common presentations, with a range between 16.7%-66.7% for ordering the recommended tests for each particular lecture break. Despite varying knowledge on diagnostic algorithms, all participants are able to come to the correct diagnosis by the end of the case. There is currently not enough data to measure statistical changes in responses among participants.

Conclusion: The launch of the HVC lecture series to the UNC pediatric residency department has been met with overall enthusiasm by both trainees and faculty members. Preliminary results show an expected trend of ordering unnecessary tests by all levels of training. Future outcomes will evaluate the effectiveness of integrating these lectures by assessing for a decrease in spending habits and an overall greater knowledge of diagnostic algorithms for common clinical presentations.

A POTENTIAL ROLE FOR AUTO-GRAFT IMMUNE CELL SUBSETS TO INFLUENCE POST-TRANSPLANT OUTCOMES IN MULTIPLE MYELOMA

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Multiple myeloma (MM) is an incurable clonal plasma cell malignancy which remains the primary indication for autologous stem cell transplant (ASCT) worldwide. Currently, data suggest that a stem cell dose at a minimum level of 2×10^6 CD34(+) hematopoietic stem cells (HSC) / kilogram of body weight is minimally sufficient for engraftment, but a contemporary study of engraftment kinetics in the era of novel mobilization strategies is lacking. Additionally, early lymphocyte recovery has been associated with improved progression free survival (PFS) after autologous stem cell transplantation in multiple myeloma (MM). In fact, the number of infused autograft NK cells was found to correlate directly with early absolute lymphocyte count (ALC) in retrospective, subset analyses. Our study aimed to characterize the impact of the graft contents including stem cell dose and non-stem cell lymphocytes present in the sample on post-transplant clinical outcome. We first characterized the relationship between stem cell dose and engraftment kinetics in 81 MM patients. Our data suggested that while increased stem cell dose had no effect on survival after transplant or absolute lymphocyte count at day 15, we showed that increased stem cell dose was associated with an increased platelet count at day 15 ($p=6.00e-05$, Spearman's $R=0.444$). We subsequently performed immunophenotypic analyses on cryopreserved apheresis samples from 27 MM patients to determine whether a particular immunophenotypic profiles correlated with early ALC and/or PFS after transplant. We investigated subsets using markers on NK cells, T cells, and B cells. Out of the phenotypic analyses performed, the single strong signal associated with an improved outcome was an inverse correlation between NKG2A expression on cytolytic CD56dim NK cells and survival ($p=0.011$, Spearman's $r=-0.480$). This suggests that reduced inhibition of NK cells through NKG2A leads to improved outcomes after ASCT. These data suggest that increasing the stem cell dose does not improve survival overall, but that it may increase the platelet count early after transplant. They also suggest that the presence of a skewed immune cell phenotype toward a more activating NK cell profile (decreased inhibition through NKG2A) within the stem cell graft could confer improved PFS. While our data did not show a correlation between stem cell dose or an increased proportion of NK cells in the graft and survival, they suggest that a less inhibited NK cell profile could mediate differences in patient outcome after transplant. Further investigation should be aimed at delineating the role of NKG2A on reconstituting NK cells following autograft, and the potential efficacy of NKG2A blockade in immune recovery and tumor surveillance in order to unlock translational avenues to increase survival in the post-transplant setting.

Determining Protective Factors in Developing Chemotherapy-Induced Cardiotoxicity Following Hematopoietic Stem Cell Transplantation

First Author: JOYCE NJORGE Chang Kim, MD Sadeer AlKindi, MD Guilherme Oliveira, MD

Introduction: Anthracycline chemotherapies are a highly effective group of anti-neoplastic agents and are first-line treatments of both solid and hematologic malignancies. However, optimal use of these drugs is limited by the complication of cardiotoxicity leading to a dilated cardiomyopathy and, in many cases, death secondary to heart failure.

The OVERCOME trial culminated in preliminary findings of protective value of combined enalapril and carvedilol therapy in patients undergoing intensive chemotherapy for malignant hemopathies. We sought to further explore and compare the benefits of varying ACE inhibitors, beta blockers, and ARBs in the prevention of cardiac dysfunction of patients prior to undergoing hematopoietic stem cell transplantation (HSCT) for hematologic malignancies. This work may allow for the utility of anthracycline chemotherapy at optimal dosage and duration for treatment of malignancies.

Methods: We prospectively enrolled 57 adult patients undergoing HSCT for hematological malignancies. Left ventricular function was assessed pre- and post-transplant using left ventricular ejection fraction and 2-dimensional global longitudinal strain. Patients were non-randomly assigned to prior treatment with beta-blockers, ACE inhibitors, or ARBs or no intervention.

Results: Of the 57 enrolled patients, 28 (49.1%) were male and the median age was 57 years (range 24-72). A total of 31 (54.4%) patients received preemptive BB treatment (12 BB, 19 BB+ACEI/ARB). Baseline LVEF and GLS were similar among groups. 6 (10.5%) patients had developed overt post-treatment cardiotoxicity ($\geq 10\%$ absolute decrease in LVEF) and 10 patients (17.5%) had subclinical cardiotoxicity ($\geq 15\%$ relative decrease in GLS). In multivariable analysis controlled for ACEI/ARB use, cardiovascular risk factors, prep regimen, and baseline GLS or LVEF, preemptive BB use was a significant predictor of lower risk for subclinical cardiotoxicity (OR=0.024, p=0.046), but not overt cardiotoxicity. When additionally controlled for chemotherapy regimen (anthracycline vs. non-anthracycline), this effect was diminished (OR=0.045, p=0.099). The number needed to treat with BB to prevent subclinical toxicity was 9.83.

Conclusions: Subclinical cardiotoxicity developed in about a fifth of patients following HSCT, with or without evidence of overt cardiotoxicity. Beta blockers may significantly reduce the risk of subclinical cardiotoxicity (OR=0.024, p=0.046). Randomized trials are needed to confirm these findings.

Incidence and outcomes after stroke on rotary flow ventricular assist device support

First Author: Jeremy Joseph MS Muath Bishawi MD Babatunde Yerokun MD David Ranney MD Patrick Winterton Jacob Schroder MD Mani Daneshmand MD Dawn Bowles PhD Joseph Rogers MD Carmelo Milano MD

Introduction: Adverse events limit benefits of Left Ventricular Assist Device (LVAD) therapy for patients with end stage heart failure. One of the most important events is stroke, as in many cases it leads to death or debilitating residual deficits that limit quality of life and functional status.

Methods: We performed a retrospective review at a single institution, of all consecutive patients that were supported on an implanted rotary flow LVAD from 2009 to 2014. Baseline characteristics were collected by chart review. Patients experiencing symptoms of a cerebrovascular event underwent a head CT. All official radiology reports were reviewed for acute ischemic or hemorrhagic stroke. As per INTERMACS, a stroke event required a new neurologic deficit with a corresponding finding on imaging. Follow-up was 100% complete, and chart review of follow-up appointments determined survival status. A logistic regression model was also built based on factors previously identified as associated with stroke including: gender, age, and device type.

Results: There were a total of 397 consecutive rotary flow LVADs implanted, (299 axial-flow, and 94 centrifugal-flow). Of those, 51 (12.8%) experienced a stroke post-implantation at an average follow-up of 3.5 ± 1.6 years. There were 0.04 stroke events per patient year, (0.03 for the axial-flow LVADs, and 0.07 for the centrifugal-flow LVADs). Of those suffering strokes, 34 (67%) were male, and 36 (70%) were for destination therapy. There was no difference in age at time of implantation between those who experienced post-operative stroke vs. those who did not (55.3 vs. 58.0, $p=0.19$). Average time from LVAD implantation to stroke was 242 ± 272 days, range (2-951 days). 17 out of 51 strokes (33%) occurred during the first year post-op, 16 (31%) occurred during the second year, 9 (18%) during the third year, and 6 (12%) during the fourth year. Overall, 34 out of 51 (67%) of patients with a stroke died during follow-up. Post-operative survival was significantly worse in patients with a post-operative stroke Chi-square 46.9, log rank <0.0001 . Gender, age, and device type were not independent predictors of stroke, although there was a trend for increased incidence in the centrifugal-flow LVAD patients ($B = -0.6$, $\text{Chi}^2 = 3.5$, $p = 0.059$).

Conclusion: Post-operative stroke was associated with significant mortality post-LVAD implantation. While the majority of strokes occurred during the first two post-operative years, ongoing risk continued after the second year. There appears to be a trend toward a higher rate of strokes per patient years for patients supported on centrifugal-flow LVADs.

Is Risk of Bias or Quality Systematically Evaluated in Cardiology Systematic Reviews and Meta-Analyses?

First Author: Dev Jaiswal Second Author: Matt Vassar

Introduction: Evidenced-based medicine is the basis of treatment guidelines. In cardiology, systematic reviews and meta-analyses are considered level 1a evidence, therefore used to make treatment-defining decisions in the field. Thus, it is crucial that these studies are further evaluated. In this study, measurement quality or risk of bias (MQ/ROB) of systematic reviews and meta-analyses were analyzed. The goal of the study was to investigate how MQ/ROB plays a role in systematic reviews and how the potential bias present affects the studies.

Methods: A PubMed search was conducted using five of the most prominent cardiology journals which were selected by impact factor using Google Scholar Metrics. The five journals selected were European Heart Journal, the Journal of American College of Cardiology, Circulation, Circulation Research, and Cardiovascular Research. With these journals, 282 articles were selected, screened through Covidence, and the relevant 182 articles were measured for quality. The methodology to evaluate quality included whether authors analyzing MQ/ROB assessed for individual studies included in the meta-analysis, MQ/ROB tool used, custom measurements to grade risk of bias, what scale was used to measure MQ/ROB, if high risk of bias or low quality was included in the analysis, if high risk of bias or low quality studies were further inspected with subgroup, meta-regression, or sensitivity analysis. Risk of bias was graded and then further analyzed by their respective journals.

Results: In this study, it was found that most authors in Cardiology do not incorporate MQ/ROB in their systematic reviews. Of the 182 articles explored, 99 studies assessed risk of bias. Of the 99 studies, 71 found a risk of bias indicated that 71.72% have some trials with questionable quality. While all authors are encouraged to assess MQ/ROB, authors using custom measurements can falsely elevate the quality of studies. These specific studies were further analyzed for the tools used, if they accurately represented quality, and compared to the standard tools used for MQ/ROB.

Conclusion: In summary, our study suggests that most authors in Cardiology do not incorporate MQ/ROB in their systematic reviews. When MQ/ROB was assessed, quality is often not fully displayed, leaving ambiguous results. Systematic reviews have pertinent implications of clinical guidelines and decision-making, therefore it is crucial to interpret whether these specific reviews maintain quality measurements. Furthermore, in order to have a more standardized approach, one of the established tools such as the Cochrane Collaboration Assessment of Risk of Bias or Newcastle-Ottawa Scale is recommended.

Knowledge Attitude Practice Regarding Vaccine Preventable Diseases in Rural area of Peshawar, Pakistan

First Author: Adnan Khan, MBBS

Introduction: The historical success of eradicating the dreaded disease, Smallpox, prompted World Health Organization (WHO) to ask its member countries to launch immunization against six vaccine preventable diseases in its national immunization schedule. In May 1974, the WHO launched the Expanded Immunization Programme (EPI) globally, with focus on prevention of six vaccine preventable diseases by the year 2000.

Methods: A community based, cross-sectional study will be conducted in the rural area of Nehaqui, Peshawar. Two villages were chosen for convenience sampling and house to house survey was done. The study was carried out over a period of one month (February to March 2015). All mothers/responsible guardians of children aged 12-23 months were included in the study. After explaining the purpose of the study to the mothers/responsible guardians, oral consents were taken. Mothers/responsible guardians who did not give consent were excluded from the study. Information regarding knowledge, attitude and practices was collected by using semi-structured proforma. Reasons for non-immunization as per the mothers' reports, were recorded. **Results:** out of 102 children 54.9% were male and 45.1% female, majority of mothers were housewives 96.1% and 81.4% were illiterate. 61.8% were fully immunized, 36.3% were partially immunized and 2% were not immunized. Main reason for partial/un-immunization was found to be lack of education regarding vaccination 32.4%, 20.6% were unaware about the importance of the vaccination. 90.2% received BCG vaccine, 94.1% received OPV, DPT were received by 92.2%, and measles was received by 68.6% and 86.3% received Hepatitis B vaccine. On Chi-Square test, it was found that the effect of factors, such as mother's educational status, sex of the child and site of immunization on the immunization status, was not statistically significant on mother education and gender of child.

Conclusion: Mass education and awareness should be done in this area. Educational interventions are needed to upgrade parents' knowledge with special emphasis on less educated and residents of rural areas. An unfortunate fact was that though a vast majority of the population recognized the importance of immunization, a superficial knowledge of the schedule and failure of the authorities in inculcating enough motivation in the target population for completing the schedule, has led to a large proportion of the children being partially immunized. Health personnel should develop a comprehensive strategy, to bring out effective changes in the attitudes and practices regarding immunization of children.

Innate Immune Sensing of the Hepatitis B Virus

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Introduction: Hepatitis B virus (HBV) remains a major public health concern with more than 240 million people chronically infected worldwide. As current antiviral treatments require lifelong medication adherence, development of more effective therapeutics remain relevant. One avenue of drug development involves induction of targeted innate immune responses. However, the interplay between innate immunity and HBV is incompletely understood. Previous studies showed negligible induction of pro-inflammatory cytokines and interferon-stimulated genes (ISGs) in the acute phase of HBV infection. Yet, recent *in vitro* studies identified RNA and DNA elements of the virus that can be sensed by various pattern recognition receptors (PRRs), such as the intracellular RIG-I receptor, suggesting the possibility of innate immune detection of HBV. Further evidence purported that antiviral nucleotide analogues (NAs) could abrogate RIG-I-mediated interferon (IFN) responses by suppressing HBV transcription (Sato *et al*, 2015). These findings hold significance in the design of antiviral drugs that aim to augment intracellular responses against HBV infection. Thus, our study aimed to clarify innate immune sensing of HBV through *in vitro* modeling of infection.

Methods: Three *in vitro* infection models (hepatoma cell lines HepG2-NTCP, stem cell derived hepatocytes, and primary human hepatocytes (PHHs)) were infected with cell-culture derived HBV (HBVcc) or HBV-infected patient sera of different viral genotypes, or transfected with replication-competent HBV plasmids. The impact of NAs on the HBV life cycle was evaluated by measuring different HBV infection markers, including viral DNA, RNA, and secreted virions and antigens. Innate immune sensing of HBV was determined from kinetics of IFNs and ISGs by qPCR. Finally, infection of HBVcc with simultaneous transfection of PRR agonists in HBV-sensitive hepatocyte cell lines was performed to determine the capacity of HBV to suppress PRR-mediated innate immune responses.

Results: NAs significantly suppressed viral replication, exhibiting little effect on viral transcription and antigen production. Furthermore, HBV infection within all *in vitro* models did not induce IFNs or ISGs above background levels. Finally, infection of HBVcc with simultaneous transfection of PRR agonists resulted in significant reduction of downstream PRR signaling molecules at multiple timepoints.

Conclusion: Our findings demonstrate that HBV can adeptly evade and actively inhibit intracellular innate immune detection within early stages of infection. This data questions the physiological relevance of PRR-mediated sensing of HBV, but also underlines the value in elucidating the virus' evasion mechanisms to guide future antiviral drug design.

Bacterial exploitation of molecular mimicry suppresses acute inflammation to promote airway infection.

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Introduction: Despite the proliferation of antibiotics and vaccines, bacterial pneumonia remains a leading cause of mortality worldwide, especially among children in the developing world. Elucidating novel immune evasion mechanisms used by respiratory pathogens may provide novel avenues for therapeutic intervention. Regulation of neutrophil responses is particularly critical for extracellular pathogens to avoid acute clearance, yet the mechanisms by which many bacteria disrupt phagocyte function remain largely unknown.

Methods: Using a murine model of upper airway infection, mass spectrometric analyses of in vivo samples, and primary human neutrophils, we tested the hypothesis that *Streptococcus pneumoniae* uses enzymes traditionally considered important for cell wall maintenance to suppress inflammation directly. Our primary outcome measures included quantification of airway bacterial loads, quantity and activation status of neutrophils present in airway lavages, and direct quantification of lipid inflammatory mediators in the respiratory tract.

Results: Here, we show that the leading respiratory pathogen *S. pneumoniae* functionally disables neutrophils by exploiting molecular mimicry to degrade platelet-activating factor (PAF), a host-derived inflammatory phospholipid. Capitalizing on phosphorylcholine (ChoP) moieties shared between its own cell wall and PAF, the microbe employs a cell wall-remodeling enzyme, Pce, to abolish PAF from the airway. PAF deprivation corresponds with marked defects in the viability, activation, and bactericidal capacity of responding neutrophils. In the absence of Pce, neutrophils clear bacteria rapidly from the airway, protect against invasive disease, and impair transmission between murine hosts. Abrogation of PAF signaling in vivo renders Pce dispensable, reinforcing that the enzyme disarms neutrophils by depriving the cells of essential PAF-mediated stimulation. Accordingly, exogenous activation of murine and human neutrophils overwhelms Pce-mediated phagocyte evasion, protecting murine hosts from pneumococcal disease.

Conclusions: These results uncover a novel mechanism by which shared molecular structures enable a microbial enzyme to subvert host lipid signaling, suppress acute inflammation, and ensure bacterial persistence at the mucosa. Ongoing work suggests mimicry-driven PAF degradation is a broadly used immune evasion mechanism among diverse respiratory pathogens that continue to exact heavy burdens of disease worldwide.

Decision-Making in Accessing the Emergency Department Versus Primary Care

Lev Malevanchik Rickie Brawer, PhD, MPH Priya Mammen, MD, MPH Bernard Lopez. MD, MS

Introduction: Visiting the Emergency Department (ED) for non-emergent health concerns is costly to the health care system and diverts attention from patients who need immediate care. In fiscal year 2011 and 2012, 95% of Thomas Jefferson University Hospitals' (TJUH) ED visits from patients living in TJUH's community benefit area (CBA) were for conditions with lower priority Emergency Severity Index (ESI) numbers of 3, 4, or 5. Many of these visits were non-emergent. The purpose of our study was to begin to address the reasons for this phenomenon.

Methods: In July and August 2013, semi-structured interviews were conducted at TJUH's EDs (including Methodist hospital) with 100 patients who live in the CBA and were categorized as an ESI of 3, 4, or 5 in the ED. A 37-question survey was administered and included both closed- and open-ended questions regarding demographics, insurance status, chronic medical conditions, and decision-making when coming to the ED. Closed-ended question responses were coded and entered into Excel. Open-ended responses were reviewed by researchers for themes and responses were coded accordingly. After reviewing the data and addressing discrepancies, responses were organized into more general categories and plotted into charts.

Results: At 52%, the most common reason patients chose the ED was difficulty in accessing primary care. At 20%, the second most common was the convenience of the ED and the desire to receive care more quickly. 79% of ED patients had both health insurance and a PCP. 56% of patients had visited an ED in the prior year. Only 36% of patients came to the ED because they believed they were having a medical emergency.

Conclusion: If TJUH seeks to increase PCP usage for non-emergent conditions, it is clear that PCPs should make it easier for patients to obtain prompt sick-visit appointments and should continue to educate the TJUH community about what types of ailments need to be seen in the ED and what types can wait for a PCP.

Erythropoietin and high fat diet-induced hypothalamic inflammation

First Author: Josue David Caban Alvarez Other Authors: Soumyadeep Dey and Constance Noguchi

Erythropoietin (Epo) is a 165 amino acid cytokine produced in the fetal liver and adult kidney and is responsive to low blood oxygen levels. It interacts with hematopoietic stem cells in the bone marrow to stimulate the production of red blood cells (RBCs), and it also plays a role in peripheral tissues to produce a myriad of extra-hematopoietic effects. Epo produced in the brain by astrocytes and neuronal cells has been proven to stimulate the differentiation and maturation of neural progenitor cells in culture and prevents ischemia-induced cell death after middle-cerebral artery occlusion in animal models. Erythropoietin receptor (EpoR) in the brain is expressed in microglial cells which can sense the presence of saturated fatty acids and release pro-inflammatory mediators in response. We hypothesized that Epo signaling in the hypothalamus acts to reduce microglial cell activation and consequently helps in the regulation of body energy homeostasis and metabolic response to a high fat-diet (HFD).

A two-week HFD regimen was administered to wild-type (WT) mice controls, transgenic mice with chronic human Epo overexpression in the brain (Tg21 mouse model), and transgenic mice with EpoR knockout localized to neuronal cells in the brain (EpoR^{NestinKO} mouse model). Hypothalamic sections were prepared with antibodies both against the inflammatory cytokine *TNF-α* and *Iba-1* (microglial marker).

Tg21 mice had significantly lower fasting blood glucose levels both at baseline and after the two-week HFD challenge, supporting our hypothesis of Epo's energy-regulating effects. To add to this effect, Tg21 mice had significantly lower weight gain, attributed to a lesser fat mass gain throughout the experiment. All of this without a significantly different hematocrit level, indicating Epo's signaling in the brain is independent of peripheral RBC numbers. In contrast, EpoR^{NestinKO} mice had significantly higher fat mass gain throughout the two-week experiment and showed an increased trend in fasting blood glucose levels. Consistent with our hypothesis, WT mouse brain sections had significantly higher microglial cells present in hypothalamic sections compared with Tg21 mice.

Epo signaling in the arcuate nucleus of the hypothalamus acts to decrease microglial cell activation and reduce the inflammatory impact mediated by a HFD regimen independently of peripheral RBC numbers.

Understanding the Role of Social Environment and Early Symptoms of PTSD in Adolescents Following Physical Trauma

First Author: Anjali Chandra MEd/ Additional Authors: Megan Ranney MD MPH, Jeff Huang PhD, Thomas Chun MD MPH, Anthony Spirito PhD, Susan Duffy MD, Nicole Nugent PhD

Introduction: Approximately 68-80% of adolescents experience a traumatic event, this percentage varying based on the sample population and definition of “traumatic event”, with 3-57% meeting diagnostic criteria for Posttraumatic Stress Disorder (PTSD). Symptoms following a traumatic event may fall under a diagnosis of Acute Stress Disorder (ASD) and/or PTSD, with a strong association between the two disorders. ASD describes acute posttraumatic symptoms occurring 2 days to 1 month after trauma, with more focus on dissociative symptoms, and PTSD describes long-term symptoms lasting more than one month following a traumatic event. Studies have shown that biomarkers of early stress, including heart rate, can be mitigated by the post-trauma social context. Studies have relied on self-reported social context, which are limited both in details and by reporter biases. Technological advancements, such as the Electronically Activated Recorder (EAR), allow more detailed characterization of the social context by recording ambient sounds and minimizing reporter bias. Our hypothesis is that adolescents who spend more time with others in non-conflictual and directly engaging social interactions following experiencing a traumatic event will evidence fewer symptoms of ASD relative to adolescents whose interactions are conflictual and disengaged.

Methods: Following IRB approval, patients between ages 13 and 17 seen at the Hasbro Children's Hospital Emergency Department with a complaint involving physical trauma were screened over 175 hours June to October 2015. Eligible participants were medically stable adolescents who required a trauma team activation, treated in a critical care room, or admitted due to injuries sustained as result of their trauma. Patients with any suicidal ideation, psychotic symptoms, or trauma involving sexual abuse were excluded. Upon discharge, recruited participants were given an EAR set to record for a duration of 30 seconds every 12 minutes and were given instructions to wear the device during the first weekend following their discharge. Participants returned 2 weeks following their discharge and completed a qualitative clinical interview as well as returned their EAR device. Participants were compensated for their participation in the study.

Results: 32 patients were screened for eligibility. Of 15 eligible patients, 8 participants were recruited and consented (7 males and 1 female). Participants that refused cited transportation constraints or lack of interest. Mean age was 15.2. A total of 453 audio recordings were obtained. Researchers screened audio files and any remarks regarding trauma or direct engagement were noted. The Acute Stress Disorder Structured Interview (ASDI) was administered by a staff clinical psychologist.

Conclusions: Among participants reporting greater symptoms at 2 weeks, audio files capture conflictual interactions between the participant and their family. Family injury-related conversations with adolescents who were more symptomatic at 2-weeks were also noted to involve comments regarding money or responsibility for participant care. These results demonstrate a positive association between conflictual social interactions and symptoms of ASD that are also early symptoms of PTSD following trauma and further extend our understanding of the quality of support necessary to support adolescents following traumatic events.

Anti-Microbial Copper Nanoparticle Film

Daniel Parrott, Michael Chaussee, Kevin Ringelman

Copper is a common metal with strong anti-microbial properties. Despite this property, it is used sparingly in health care due to the great effort and cost associated with retrofitting hospital surfaces with copper sheet metal. These problems are surmountable, however, as films of copper nanoparticles embedded in a polymer matrix offer a cheaper, easier, and at least as effective alternative. In this pilot study, we created films of copper nanoparticles embedded in a polyvinyl butyral (PVB) polymer matrix, and demonstrated that these films have superior anti-microbial properties to copper metal plates.

To create films, we made solutions of 16.7% PVB in glacial acetic acid, and dispersed spherical, 10 micrometer diameter copper nanoparticles into the solution at a mass ratio of 2:1 nanoparticles to PVB. We used a Meyer rod to evenly coat the solution over a plastic film. Next, we created bacterial solutions of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Streptococcus pyogenes*. We pipetted 20 microliters of diluted, quantified bacterial solution on the film for specific exposure times, swabbed the film, and transferred the swab to an agar plate. The plates were allowed to grow overnight and colony forming units (cfu) were counted.

Because this was a pilot study, the goal of the experiment was to demonstrate internal consistency of the data and not generate robust statistics; thus only the experiments with *S. aureus* were replicated for concrete statistical analysis. At two minutes of bacterial exposure time on the nanoparticle film, there was an average of 0.73 logs of cfu, compared to 4.25 logs of cfu on the metal plate ($p < 0.05$). At five minutes of bacterial exposure time on the nanoparticle film, there was an average of zero cfu compared to 1.31 logs of cfu on the metal plate ($p < 0.05$). Overall, no *S. aureus* cfu were counted after three minutes exposure time on the nanoparticle film compared to ten minutes on the metal plate. For *S. Pyogenes* no cfu were counted after two minutes of exposure time on the nanoparticle film. In contrast, it took ten minutes on the metal plate before no cfu were counted. The plate and film had essentially identical anti-microbial activity against *P. aeruginosa*, with no cfu present after five minutes. In all experiments, a plastic laminate was used as control, and it displayed growth several orders of magnitude greater than the copper substrates.

Our data, particularly *S. aureus*, demonstrates the superiority of nanoparticle film over copper metal plates. Though we used a Meyer rod in this experiment, the nanoparticle solution can easily be spray-coated on hospital surfaces, reducing the number of hospital acquired infections and saving lives.

Quality Improvement of Food Insecurity in the Kansas City Metropolitan Area

First Author: Seyed Khalafi Second Author: Raj Shah Third Author: Felicia Ratnaraj Fourth Author: John Foxworth

Introduction: Over 1 million people in the state of Missouri have low food security, which is defined as problems or difficulties accessing sufficient food. The Kansas City Metropolitan area households had 15.9% food insecurity as of 2013, higher than the state average of 13.9%. Second Servings, a student led service project interested in fighting hunger in Kansas City, was developed and has aided in fighting malnutrition and disease in the area by feeding the underprivileged and promoting healthy lifestyles.

Methods: Ten students on a monthly basis met to pack meals for an hour. The organization started off with a grant of \$1,800 from AOA that was used solely for purchasing food items to be included in the meals. These meals included non-perishable items such as one protein, grain, milk/dairy, snack, fruit, and a water/drink item. These meals were packed at UMKC SOM and later taken to Sojourners Health Clinic, a free health clinic in the KC area, to be distributed to the patients.

Results: Since 2012, the result of the student led intervention has allowed over 800 individuals to be fed at the free health clinic in the greater Kansas City area. The average meal costs \$2.63 per person in the Jackson county area. Through the intervention, each meal cost approximately \$1.57.

Conclusion: Further encouragement should be done for motivated students to participate in student led healthy eating interventions to impact the community with healthier and more affordable lifestyle options.

Temporal characteristics of missed clinic appointments in an academic center in west Texas

First Author: Cheyenne M Mangold Jeff Dennis, PhD Mark Dame, MHA Tom Xu, MD PhD Cynthia Jumper, MD MPH Alan Peiris, MD PhD

Background: Missed clinic appointments have a negative impact for both the patient and the clinic. Lost opportunities for teaching as well as lost revenue occur. Moreover, it perpetuates longer waiting times for clinic consultation and often results in overbooking which has the potential to lead to patient and provider dissatisfaction. Patients that miss clinic appointments are also likely to have poor health outcomes, incomplete preventative screening, and greater use of emergency care. This study evaluates factors linked to missed clinic appointments.

Methods: Data selection included all missed appointments from 2010-2014 in the Internal Medicine clinic at Texas Tech Health Sciences center in Lubbock. All individuals, aged 18 and over, with at least one clinic no show were included in the analysis. A transact-SQL query was used to pull data from the Cerner and Centricity databases. Data was matched via medical record number and combined into a single database. The final sample included 162,000 appointments, linked to 18,023 individuals. Statistical significance was set at the $p < 0.05$ level. Except where noted, holidays are defined as weekdays where the clinic was closed.

Results: Data were analyzed to determine what appointment characteristics are linked to clinic no shows. Twenty-five percent of all appointments were missed. No shows after 3 p.m. were highest (28%), while appointments 10 a.m.-noon were lowest (23%). No show rates for Monday through Thursday ranged from 24.5-25.5%, whereas the Friday no show rate was 29%. Additionally, Tuesday afternoons had significantly higher no show rate (29%), similar to Friday afternoon. No shows on days after holidays were also particularly high, at 29%. Further, no show rates after “fixed” holidays, i.e., those always falling on a Monday, were significantly lower (27.9%), compared to no show rates after “floating” holidays (30.9%).

Appointments on the day before a holiday had a significantly lower no show rate (26.7%) than days after holidays, and rates dropped further with Fridays excluded (24%). Finally, appointments on common federal or religious holidays when the clinic was open, e.g., Good Friday, exhibited a no show rate of 25.7%, resembling average non-holidays, and significantly lower than days after holidays when the clinic had been closed.

Conclusion: Days following holidays exhibited the highest no show rates, and may be conducive to overbooking or additional appointment reminders. If Friday afternoons were scheduled exclusively for walk in clinics, no show rates might improve. Further, if extended hours were available Monday through Thursday, patient needs may be better accommodated. Reduction of missed appointments stands to improve cost and time efficiency for health care providers and promote continuity of care for patients. Findings suggest that clinics need to study no show patterns to understand potential regional and national differences that impact appointments.

Upper Gastrointestinal Bleeding (UGIB): Can we improve our Management?

First Author: Stephanie Ossowski, MS-4 (ACP Student Member); Alexander Bullen, MD; Michael Maloy, MD; James Hanley, MD, FACP

Introduction: UGIB is a common cause of inpatient admissions often associated with morbidity and an overall mortality rate approaching 10%. Since therapy is different, it is important to differentiate between variceal and non-variceal GI bleeding. While both will often need volume resuscitation, proton pump inhibitors (PPI), judicious transfusion and early endoscopy, patients with variceal bleeding will need other intervention to include antibiotics and vasoactive agents. We were interested in whether we followed the guidelines and whether we could make recommendations to improve our care.

Methods: A retrospective analysis was performed on admission and discharge data from January 1, 2013 to January 31, 2014 of patients admitted to our hospital with a diagnosis of UGIB. Patients with a history of malignancy were excluded. Data regarding source of GI bleeding, number of patients transfused, hemoglobin/hematocrit upon presentation, history of previous gastrointestinal bleeding, number of patients who developed complications post-transfusion, number of patients who received PPIs, number of patients who received vasoactive agents, number of patients with hepatic cirrhosis who received antibiotic prophylaxis, and number of patients in which overall management was adequate, was obtained.

Results: A total of 100 patients met criteria. 54% were male, and the average age for men was 67 years old and 69 for women. 12% of the patients had hepatic cirrhosis. 37% of the patients had CAD. 62% of the patients were transfused. 4% of the patients experienced complications to transfusions. 26% had a history of prior GI bleeding. Only one (9.0%) of the patients with hepatic cirrhosis presenting with UGIB received antibiotics. Five (15%) of the patients with CAD who were transfused had an Hb greater or equal to 10 g/dL. Only ten (28.6%) of the patients without CAD were transfused according to the current guidelines.

Conclusion: We found that our management was suboptimal 39% of the time. The principle cause of suboptimal care was overuse of blood transfusion and underuse of antibiotics in cirrhotic patients. Current guidelines emphasize restrictive transfusions, since it leads to reduced rates of further bleeding and need for rescue therapy. Appropriate use of transfusion is also cost-effective, with the cited cost of a platelet depleted red blood cell unit to be as much as \$2,400. Among cirrhotic patients, the prophylactic use of antibiotics was low. There have been multiple trials that have shown an overall reduction of infectious complications and decreased mortality (NNT=16) with the use of prophylactic antibiotics. These findings have been reported to the Quality Improvement Committee, with recommendations on the use of transfusions and antibiotics in these patients.

Depression and Oxytocin dose: correlation during Labor

First Author: Muhammad Yasin Hira Burhan Syed Askari Hasan Zohaib Ahmed Haseeb Zubair Faiza Abdul Jabbar

Objective: To investigate the relationship between depression during pregnancy and dosage of oxytocin required during labor.

Study design: This cross-sectional study was conducted on 100 pregnant women in Abbasi Shaheed Hospital, Obstetrics & Gynecology unit I and OPD between August and December, 2012. Depression level was evaluated by applying Patient Health Questionnaire (PHQ-9). Later on, these women were followed in the labor room to assess the dosage of oxytocin they required during labor. SPSS 16.0 was used for data entry and analysis.

Result: Study was carried out on 100 pregnant women with a mean age of 25.59 ± 3.97 . A total of 95% (n=95) of females were presented in third trimester. An oxytocin dose of 15U/L was required in women with a mean PHQ score of 10.52 ± 2.22 while doses of 10U/L and 5U/L were required in women with a mean PHQ of 8.41 ± 4.28 and 3.40 ± 2.88 respectively. There was a statistically significant difference among groups as determined by ANOVA [$p < 0.001$] and confirmed through post-hoc tests. The strength of association between oxytocin dose and PHQ score is moderate ($r = 0.425$), and the correlation coefficient is significantly different from zero ($P < 0.001$).

Conclusion: A higher dose of oxytocin could improve overall performance during labor in depressed women and is useful in avoiding complication associated with prolong labor.

MOLECULAR MECHANISM OF CELLULAR STRESS AND APOPTOSIS INDUCED BY INHIBITION OF SIAH E3 LIGASE FUNCTION IN HUMAN CANCER CELLS

First Author: Dasom Lee Additional Authors: Monicah M. Njogu, and Amy H. Tang, Ph.D

INTRODUCTION: EGFR/HER2/K-RAS hyperactivation is prevalent in metastatic cancers, responsible for 90% of cancer-related deaths. Many anticancer therapies that control and inhibit this pivotal tumor-driving pathway have been developed but not yet achieved clinical efficiency in clinical oncology. To address this problem, we identified the most downstream player of the EGFR/HER2/K-RAS pathway called E3 ubiquitin ligase seven in absentia (SIAH2). We showed that inhibiting SIAH2 function blocked K-RAS-dependent tumor growth in human pancreatic and lung cancers, demonstrating the role of SIAH2 as a novel therapeutic target in K-RAS-driven cancers. (Schmidt et al, 2007 and Ahmed et al, 2008). To further elucidate SIAH2 function, we investigated the molecular mechanism of how SIAH2 loss of function induced cellular stress and apoptosis in HeLa and MDA-MB-231 cells.

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METHODS: We used the DOX-inducible Tet-ON stable line expression system to introduce SIAH2^{PD}, a proteolysis-deficient mutant protein and a competitive inhibitor of SIAH2, and thus made the cells treated with doxycycline lack proper SIAH2 function. Then the cell apoptosis induced by anti-SIAH therapy was evaluated by Annexin V-FITC/propidium iodide (PI) staining; flow cytometry was used to measure cell viability in the treated cells. Production of intracellular reactive oxygen species (ROS) induced by anti-SIAH therapy was measured by fluorescence microscopy using 2', 7'-dichlorofluorescein diacetate (DCF-DA).

RESULTS: Compared with their control groups, anti-SIAH therapy treatment caused a marked increase in apoptosis in both HeLa and MDA-MB-231 cells. A prominent ROS production was induced by anti-SIAH therapy in HeLa cells, but not in MDA-MB-231 cells.

CONCLUSION: Anti-SIAH therapy effectively induced apoptosis in both HeLa and MDA-MB-231 cells. To examine anti-SIAH therapeutic efficacy in multiple cell lines, in future, we hope to delineate SIAH2 function, identify cancer subtypes that are sensitive to anti-SIAH therapy, and offer a novel and logical strategy to halt cancers driven by EGFR/HER2/K-RAS activation.

The Effects of Betatrophin on Beta Cell Mass and Glucose Homeostasis in 12-Lipoxygenase Knockout Mouse Model, a Pilot Study.

First Author: Sichen Liu Second Author: Wojceich J. Grzesik Third Author: Lindsey Glenn Fourth Author: Jerry Nadler Fifth Author (PI): Yumi Imai

Background: In type 1 diabetes (T1D), autoimmune mediated reduction of pancreas beta cell mass correlates with clinical progressions of the disease. Previous studies show that 12-lipoxygenase (12-LO) contributes to beta cell loss in diabetes via inflammatory lipid mediators, while mice deficient of 12-LO are protected against the development of diabetes in non-obese diabetic (NOD) mice, a T1D animal model. Recently, a liver hormone called betatrophin has been implicated in both increasing beta cell mass and improving glycemic control.

Objective: To evaluate the synergetic effect of betatrophin with 12-LO suppression via 12-LO knock-out NOD (12-LOKO) mice.

Experimental Design: Two cohorts of five female 12-LOKO mice were injected with adenovirus vectors (1.1×10^9 IFU/mouse) carrying GFP or betatrophin. The mice were kept in healthy condition during the two week experimental period. Insulin and glucose tolerance tests were conducted on day 7 and day 10, respectively, and measurements were done with tail vein blood. Pancreas and liver were harvested at the end for the measurement of beta cell proliferation (BrdU incorporation), islet area, and betatrophin expression.

Results: All mice did not develop diabetes. Overexpression of betatrophin protein in the liver of the betatrophin cohort ($p < 0.05$ vs GFP control, $n = 5$ per group). Mice overexpressing betatrophin showed trend of lower blood glucose (BG) levels in both Glucose Tolerance Test and Insulin Tolerance Test. Betatrophin group displayed a trend of lower serum insulin after 4 hours of fast, while it displayed a statistical-significant lower BG level (94 mg/dl vs 150 mg/dl in GFP, $p < 0.05$) against the GFP group after 4 hours of fast. Histological study of pancreatic sections indicated the betatrophin group showed trends of increase in beta cell area (0.6% of islet-area vs 0.21% in GFP, $p = 0.13$), beta cell number (17 BrdU+ cells vs 6.4 in GFP) and beta cell proliferation (1.1×10^{-4} % of islet-area vs 0.59×10^{-4} % in GFP, $p = 0.08$).

Conclusion: Our pilot, using an animal model with lower inflammatory mediators, indicates that betatrophin will likely be a weak stimulator of beta cell proliferation and likely have mild effect on glucose homeostasis. Developing a therapy that reduces 12-LO will help reduce inflammatory beta cell loss, but in established diabetes, where beta cell mass is already low, a more potent beta cell growth factor will need to be developed.

Efficacy of Patient Teach-Back in Improving Patient Adherence in the Outpatient Primary Care Setting

First Author: Hitesh H. Patel, MS, MBA Second Authors: Robert MacGregor Parth Shah Devon Shick, MD

Introduction: Twenty-five percent to fifty percent of patients are non-adherent. Non-adherence costs the United States \$100 to \$289 Billion annually and causes 10% of hospital admissions. The National Quality Forum and The Joint Commission recommend the use of the “teach-back” method to assess and improve patients’ understanding of their treatment plan, as a way to reduce non-adherence. The method involves asking patients to repeat back key points of the treatment plan to determine what the patient has learned from the health education session. It provides an opportunity for healthcare providers to address misunderstandings and target individual needs. We hypothesized that the teach-back method will improve medical adherence; to our knowledge there has been no published study looking at this phenomenon.

Methods: All patients were seen at Cedar Medical Associates, an outpatient family medicine practice over a 4-week period. Twenty-eight patients were consented for follow-up in both the control and intervention groups. The first two weeks of data collection served as the control group of the study, in which the medical team developed and educated the patients on the diagnoses and treatment plan based on their personal style and preference. The patients then received a follow-up phone call two days after the encounter. During the phone call, the patient was asked a total of five questions to assess medical adherence such as “have you filled any prescriptions you received during your visit?”

During the second two weeks of data collection, the treatment team implemented the teach-back technique. The technique was repeated until the patient could successfully state their diagnosis and treatment plan with strong understanding. This group was also received a follow-up phone call two days after the encounter and were asked the same 5 questions as the control group during the interview. The patients’ responses were scored either 1 or 0 based on if they felt their condition improved, accurately named each diagnosis, name each portion of their treatment plan, and filled every prescription. Patients only received a score of 1 in each question if they completed it fully. For example, if they forgot to a portion of their treatment plan, they received a score of zero for that question.

Of the 28 patients consented in both the control and intervention groups, follow-up calls were successfully completed for 15 patients in the control group and 10 patients in the intervention group. The data was then scored according to the protocol outlined above. The data was statistically analyzed utilizing a two-tailed Fischer’s Exact Test.

Results: As demonstrated in prior studies, this data showed that the teach-back method and motivational interviewing methods significantly increased patient knowledge acquisition and retention ($p = 0.05$). However, this study exceeded prior studies by also showing that the teach-back method led to significantly increase medical adherence to the treatment plan and filling prescriptions ($p = 0.001$). The intervention group had 100% medical adherence, whereas the control group only had 33% medical adherence.

Conclusion: Unfortunately, only 35% of physicians regularly utilize the teach-back method. However, this study has shown that the teach-back method significantly increases medical knowledge acquisition/retention and medical adherence. Further randomized controlled studies on larger sample populations should be conducted to discern if the study’s findings are replicable and generalizable. If the data is replicable, the barriers impeding physicians from regularly utilizing the teach-back method should be investigated.

Hypoxia Results in White Matter Immaturity in a Piglet Model of Congenital Heart Disease

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Introduction: Congenital heart disease (CHD) is the leading birth defect, affecting almost 1% of births each year. Full-term infants with CHD display subnormal brain development, underlying impairments in fine/gross motor skills, language, memory, and attention. Neuroimaging studies show that CHD infants have a high incidence of brain injury; partly due to insufficiencies in cerebral oxygen delivery *in utero*.

Diffusion tensor imaging (DTI) studies have revealed that white matter (WM) immaturity is common in infants with CHD. Fractional anisotropy (FA) is one measurement of DTI that reflects the degree of axon myelination. FA values rise with an increase in myelination, but are lower than normal in cases of WM injury. CHD patients have been reported to have significantly lower FA values the corpus callosum (CC), which consists of axons that connect the left and right hemispheres of the cerebral cortex, enabling interhemispheric integration of motor, sensory, and cognitive information.

White matter (WM) development occurs extensively from midgestation to postnatal year two, during which there is robust oligodendrocyte (OL) proliferation, differentiation, and myelin sheath formation around axons. OL maturation and subsequent myelination involves four lineage transitions: OL progenitor, pre-OL, immature OL, and mature OL. Different cell-specific antibodies can identify OLs at each stage of this progression.

Due to technical and ethical difficulties, the effects of CHD-induced brain injury on the cellular level remain elusive. To emulate the insufficient cerebral oxygenation in CHD, we developed a porcine chronic hypoxia model and analyzed the microstructural and cellular effects of CHD on/in the CC with DTI and immunohistochemistry, respectively.

Methods: Fixed porcine brains were imaged with a 3T-magnet at Johns Hopkins University. The cerebrum was isolated from DTI images using ROI Editor and fiber tracking was performed using DTI Studio. The primary antibodies used were PDGFR- α to label OL progenitors, CC1 to label mature OLs, Casp3 to label apoptotic cells, and Ki67 to label proliferating cells. To ensure an unbiased assessment, cell counts were performed using Stereology.

Results: DTI analysis demonstrated that hypoxia leads to a global reduction in the number and length of WM fiber tracts along with a global decrease in FA—a metric of WM integrity and maturity. Immunohistochemical analyses revealed a 75% decrease in the density of apoptotic mature OLs and an 85% decrease in the density of proliferating OL progenitors in the CC following hypoxia ($p < 0.05$).

Conclusion: Together, these findings indicate an OL lineage-specific vulnerability to hypoxic exposure where OL progenitors fail to generate new OLs at a rate necessary for normal brain development. Hence, therapies aimed at restoring the regenerative capacity of resident OL progenitors within the CC offer promising avenues to improving neurological outcomes in the growing CHD population.

Bone Marrow Registration and Donation Perceptions of Healthcare Professionals and Students

First Author: Andy Tien, MS Second Author: Joshua Hudson, MS Third Author: Christopher Theroux, MS Fourth Author: Ian Chen, MD, MPH

Introduction: A significant number of individuals who seek a bone marrow transplant are unable to find a suitable match. Healthcare professionals and students are most likely to provide advice to potential donors about bone marrow registration and donation and should be the most educated. However, many healthcare providers are misinformed about bone marrow donation and many do not want to donate because of misconceptions about the process.

Methods: We surveyed 235 healthcare professionals (MDs, PAs, NPs, RNs) and 222 health-professions students from Eastern Virginia Medical School, Sentara Norfolk General Hospital, and Children's Hospital of the King's Daughters in Norfolk, Virginia using an online platform to assess their knowledge, attitudes, and behaviors towards the bone marrow registration and donation process. Data was analyzed using chi square and logistic regression to assess significance between participant professions and between participants registered and not registered for the bone marrow registry.

Results: We received 437 responses, of which 35.5% (n=162) were male and 64.5% (n=295) were women. Of those responses, 28.9% (n=132) were registered for the bone marrow registry and 48.6% (n=222) cited that they had not been educated about bone marrow donation before. In regards to registration for bone marrow, 45.95% (n=210) said cheek swab is required, 29.54% (n=135) said blood draw is required, and 31.05% (n=151) don't know. As for the bone marrow donation process, 80.31% (n=367) believe that needle aspiration is required, 33.04% (n=151) believe that blood draw is required, and 21.01% (n=96) don't know. Students and nurses are less likely to have been educated about bone marrow donation (p=0.023). The most common reason cited for not joining the registry is being unaware of the process (20.79%, n=95) while the most common reason that may prevent respondents from donating bone marrow is time (28.23%, n=129). Those not registered are more likely to think marrow donation is painful (p=0.001), they are not needed (p=0.000), and they will be asked to donate (p=0.000). Of those not in the registry, 64.62% (n=210) agree or strongly agree that they would be more open to donating if they had more information about the process.

Conclusions: Healthcare professionals and students have misconceptions or are unaware about the bone marrow registration process, which may be a barrier to increasing the number of registered bone marrow donors within and outside the healthcare community. Additional efforts must be expended toward educating healthcare professionals and students about bone marrow registration and donation.

Detecting Pancreatic Cancer in the Blood

Nainika Nanda, Maryam Al Eissa, Anup Sharma, Nita Ahuja

Pancreatic cancer is the fourth leading cause of cancer deaths in the United States. The high mortality is underscored by the absence of specific symptoms in early disease stages and generalized gastrointestinal symptoms in late stages. Disease is currently incurable – resistance, metastasis, and organ invasion make chemotherapy and surgery poor options. There is currently no reliable early detection method for pancreatic cancer. Circulating DNA, present in higher concentrations in cancer patients, can be harnessed as a biomarker for early detection by focusing on cancer-specific epigenetic changes. These cancer-specific epigenetic changes include the methylation of CpG islands in promoter regions of tumor-suppressor genes. Targeting cancer-specific methylation changes in circulating DNA is proven for early detection of pancreatic cancer using genes ADAMTS-1 and BNC1¹. In the development of these two biomarkers, other potential biomarkers were identified. This study focused on further developing other potential markers with increased methylation frequency in plasma from pancreatic cancer patients. The goal is development of a gene panel with increased sensitivity and specificity.

Patients were categorized into control (n=48), chronic pancreatitis (n=5), IPMN (n=8), and cancer (n=20) groups. DNA was extracted from patient plasma utilizing the MOB (methylation on beads) technique. Bisulphite treatment was performed simultaneously with DNA extraction in a single tube. qMS-PCR (quantitative methylation specific polymerase chain reaction) was conducted on eluted DNA and analyzed using delta Ct method to determine methylation frequency of genes of interest – A and B.

Biomarker methylation of the genes of interest (Gene A & Gene B) was present in all stages of pancreatic cancer (Gene A: stage I=25%, stage II=80%, stage III=13%, stage IV=0%) (Gene B: stage I=100%, stage II=100%, stage III=88%, stage IV=100%). Methylation was present for Gene B in high and intermediate stages of IPMN (high=100%, intermediate=50%). Biomarker methylation was evident in chronic pancreatitis (Gene A=20%; Gene B=80%) and control patients (Gene A=33%; Gene B=52%) as well.

Circulating DNA has shown promise as a noninvasive tool for earlier pancreatic cancer detection utilizing cancer-specific methylation changes. MOB is a unique platform for conducting DNA extraction and bisulfite conversion, maximizing acquisition of circulating DNA. However, biomarker presence in control patients demonstrates that primer and probe design is not sensitive and specific enough to differentiate between cancer and control patients. Therefore, re-designing of primers and probes is necessary to target more cancer-specific methylated regions of genes of interest, and further qMS-PCR assay standardization is required.

References:

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Hepatitis B Prevalence in the Milwaukee Hmong Community

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INTRODUCTION: Although the United States is considered a low endemicity region for hepatitis B and has had low hepatitis B prevalence rates (0.3%) since the implementation of routine vaccination for newborns in 1991, the Hmong population in the U.S. has rates of up to 20% according to prior studies in California, making hepatitis B a prominent ethnic health disparity affecting the Hmong-American community. Based on the 2010 Census, the Hmong population in the Milwaukee-Waukesha-West Allis area numbers 11,904, making it the fourth-largest Hmong population of all major metropolitan areas in the nation. However, prior to our efforts, there had never been an attempt to determine the prevalence of hepatitis B in the Milwaukee Hmong community. Our aims were two-fold: to conduct Milwaukee's first-ever series of free hepatitis B screening and education events in the Hmong community, and to determine the prevalence of hepatitis B in this high-risk population.

METHODS: From 2013-2015, we organized a total of five hepatitis B screenings in the Milwaukee Hmong community. We utilized various locations such as local Hmong markets, churches, and festivals in order to maximize our number of screening participants. To advertise the screenings, we posted fliers at local restaurants/markets and aired hepatitis B segments on the local Hmong radio station. At the screenings, participants filled out a personal information and demographic form, answered a survey about basic hepatitis B knowledge, received a 10-15 minute educational session from a health care provider or trained coordinator, and had their blood drawn. All blood samples were centrifuged on-site and sent to LabCorp in Chicago to be tested for hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (HBsAb).

RESULTS: In total, 176 participants were screened over five events. 18 participants (10.2%) tested positive for hepatitis B infection (HBsAg +, HBsAb -). 51 (29%) were non-immune and designated "susceptible" to infection (HBsAg -, HBsAb -). 102 (58%) were immune (HBsAg -, HBsAb +) and 5 (2.8%) were designated as "gray zone" (HBsAg -, low HBsAb titers).

CONCLUSION: Based on our screening results, the prevalence of hepatitis B in our screening population was 10.2%. Although lower than the 20% prevalence rate documented in prior studies, there is still a disproportionately high prevalence of hepatitis B in the Milwaukee Hmong community compared to the general U.S. population. Equally important, 29% of our screening population was still susceptible to being infected with hepatitis B. Given these data, it is clear that hepatitis B is an important health disparity worth addressing in the Milwaukee Hmong community, and efforts to promote hepatitis B awareness, education, and when indicated immunization are warranted.