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On The Cover: Three students in anatomy class study a skeleton (Jan 1951). Image supplied by courtesy of Drexel University College of Medicine Legacy Center. For more information visit archives.drexelmed.edu

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Editorial Staff

Affiliates:

Editorial Policy

The *DrexelMed Journal (DMJ)* features the scholarly activities of our graduate medical education trainees. This journal was created to highlight the many interesting and diverse scholarly activities and research at Drexel University College of Medicine and its participating affiliates (listed above). Recognizing that scholarly activity takes many forms, the *Journal* aims to publish all such efforts, and welcomes original research, reviews, case reports, and technical reports alike.

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The lead author must be in a current, Drexel-affiliated, graduate medical education program either as a resident or fellow, (i.e. PGY-1, etc.) and must be in good standing with the program. It is the responsibility of the lead author to review the submission(s) with all listed authors prior to the final electronic submission to *DMJ*. *DMJ* does not assume any responsibility for the addition or omission of authors. It is the responsibility of the lead author to verify all conflicts of interest for every author listed on the paper.
If residents from another institution would like to participate, they should request their designated institution official (DIO) to communicate directly with the editor.

Please refer to the *DrexelMed Journal* website for further detailed instructions regarding submission guidelines:
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Please refer to the *DMJ* website for further instructions on how to submit your work for next year's edition.
All requests for reprint permission can be addressed to: DrexelMedJournal@Drexelmed.edu.

DEAN'S RECOGNITION

Congratulations to Dr, Amori for the 2017, edition of the DrexelMed Journal. Our residents and fellows demonstrate year after year that research and scholarly activity is a priority at Drexel University College of Medicine and our affiliate GME sites. We also celebrate the opportunity to showcase the faculty collaborators and mentors who help guide these young physicians in their work.

My personal appreciation to the many residents represented in this edition of the DrexelMed Journal and to those of you in training who have ongoing scholarly activities. Academic inquiry through research and innovation is part of our basic mission at Drexel. We hope throughout your training programs and your professional careers that you continue your endeavors to move medicine forward.

Daniel V. Schidlow, MD
Annenberg Dean and Senior Vice President, Medical Affairs
Drexel University College of Medicine

EDITOR'S COMMENTS

It is a pleasure to present the 2017 edition of the DrexelMed Journal. The house staff of Drexel University College of Medicine at Hahnemann University Hospital and our affiliate staff have once again submitted a wide variety of research and scholarly work across the disciplines in medicine. As always, we appreciate the work of our trainees and their mentors and collaborators in the pursuit of academic and clinical excellence. We once again celebrate the work of everyone at Drexel University College of Medicine.

Renée Amori, MD
Editor-in-Chief
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Associate Program Director, Endocrinology Fellowship
Drexel University College of Medicine

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Hahnemann University Hospital

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Associate Dean of Graduate Medical Education
Professor of Emergency Medicine
Drexel University College of Medicine

Poem: The Final Exam

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*Drexel University College of Medicine: Internal Medicine
**Columbia University: Department of Medicine

06:56:04PM: A resident tells a family, “I’m here if you need anything. We’ll make sure he’s as comfortable as possible.”

07:58:52PM: The resident is at the nurse’s station. A nurse interrupts her, “It’s time for you to go in.”

08:00:24PM: The resident says softly, “I need to do a physical exam now to confirm his passing.” The mother looks on.

08:01:11PM: The resident places a stethoscope on the patient’s chest, the other hand around his wrist, searching for any sign of a heartbeat. The mother looks on.

08:01:41PM: The resident moves the stethoscope to the periphery of the patient’s chest, listening for respirations. The mother looks on.

08:02:11PM: The resident pulls a penlight from her pocket and shines the light into each pupil, looking for pupillary reaction. The mother looks on.

08:02:24PM: The resident looks up at the clock. To the nurse: “Time of death: 8:02PM.” To the mother: “I’m so sorry for your loss.” The mother looks on.

11:53:02PM: A daughter lies awake in bed, thinking about dying in a busy hospital. She hopes maybe her loved ones can die somewhere else.

Clinical Case Abstracts

1.Ulcerated Congenital Nodule in a Neonate

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Introduction: Infantile myofibromatosis (IM) is a rare condition characterized by mesenchymal cell proliferation1. Nonetheless, it is one of the most common fibrous tumors of infancy and can be associated with systemic involvement2. **Case**: A 1-month-old African-American baby girl presented with a congenital ulcerated nodule on her left thigh. Her family history and past medical history were unremarkable. Examination revealed a 1.3-cm x 1.3-cm domed, pink, shiny, mobile, firm nodule with violaceous rim and central ulceration. She had no cervical, axillary, or inguinal lymphadenopathy. Histopathology revealed smooth-muscle actin-positive spindle-cells arranged in fascicles. **Discussion**: Infantile myofibromatosis (IM) is a rare condition characterized by mesenchymal cell proliferation. Classic histopathology findings consist of spindle-shaped cells with staining characteristics between fibroblasts and smooth muscle cells1. Three variants have been described (solitary, multi-centric, and generalized) although no histologic difference can be appreciated2. Familial patterns of inheritance have been proposed with autosomal dominant IM resulting from a PDGFR-B mutation3 and autosomal recessive IM resulting from a NDRG4 hemizygous variant4. Prenatal ultrasound may help identify lesions and diagnose the condition in utero5. Most solitary lesions may be managed with close observation, as the majority involute; however, in this case the patient had the tumor excised due to lesion size and discomfort of the ulceration. No consensus exists on the need for systemic imaging for solitary lesions2; however, she underwent a skeletal survey and abdominal ultrasound, which revealed no visceral or bony involvement. This disorder should be considered when evaluating a child with a soft tissue tumor.

Figure 1: 1.3 cm x 1.3 cm domed, pink, shiny, mobile, firm nodule with a violaceous rim and central ulceration

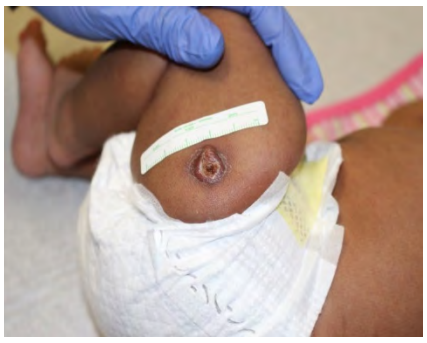
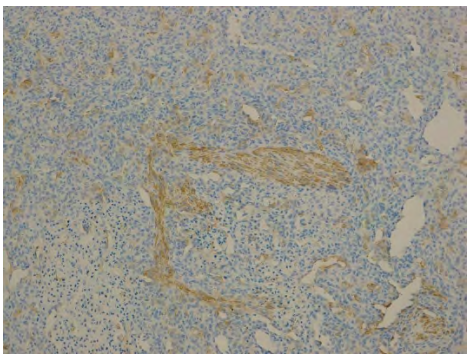


Figure 2: Smooth muscle actin positive spindle cells (100x, SMA)



Ref. 1. Cheung EB, Enzinger FM. Infantile Myofibromatosis. Cancer. 1981; 48(8): 1807-818.
2. Mashiah J, Hadj-Rabia S, Dompmartin A, Harroch A, Laloum-Grynberg E, Wolter M, Amoric JC, Hamel-Teillac D, Guero D, Fraitag S, Bodemer C. Infantile Myofibromatosis: A Series of 28 Cases. Journal of American Academy of Dermatology. 2014: 71 (2): 264-70.
3. Martignetti JA, Tian L, Li D, Ramirez MC, Camacho-Vanegas O, Camacho SC, Guo Y, Zand DJ, Bernstein AM, Masur SK, Kim CE, Otieno FG, Hou C, Abdel-Magid N, Tweddale B, Metry D, Fournet JC, Papp E, McPherson EW, Zabel C, Vaksmann G, Morisot C, Keating B, Sleiman PM, Cleveland JA, Everman DB, Zackai E, Hakonarson H. Mutations in PDGFRB Cause Autosomal-Dominant Infantile Myofibromatosis. The American Journal of Human Genetics. 2013; 92(6): 1001-007.
4. Linhares ND, Freire MC, Cardenas RG, Pena HB, Bahia M, Pena SD. Exome Sequencing Identifies a Novel Homozygous Variant in NDRG4 in a Family with Infantile Myofibromatosis. European Journal of Medical Genetics. 2014; 57 (11-12): 643-8.
5. Zhang F, Cheng D, WU M, GE L, MA X. Diagnosis of Infantile Myofibromatosis with Pseudo-ulcerated Plaque Using Prenatal Ultrasound: A Case Report. Experimental and Therapeutic Medicine. 2014; 8: 1769-771.

2.Spontaneous arterial dissections in postpartum period

Wajahat Humayun, MD, Ali Ghani, MD*, Irfan Ahsan, MD*, Ganesh Gajanan, MD*, Bruce Klugherz, MD**
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**Abington Memorial Hospital: Department of Medicine, Division of Cardiology

Introduction: Vascular diseases like aortic dissection and aneurysm including aortic, cerebral, and splenic artery involvement has been widely reported during pregnancy and puerperal period(1). The exact etiology is unknown. Below is a very interesting case of an Asian woman who presented to ER with chest pain and head ache and was found to have acute coronary and carotid arterial dissection.

Case: A 31 years old female with no past medical history and recently delivered a healthy baby 10 days ago presented to ER with new sub sternal chest pain radiating to left arm and neck along with chronic head ache. Initial EKG showed ST segment elevation in leads V4, V5 and V6 along with reciprocal depression in inferior leads II, III and aVF. Emergent coronary angiogram was performed which showed acute dissection in left anterior descending artery on which percutaneous intervention was performed with 2 drug eluting stents. Post procedure her chest pain resolved but she had persistent head ache which prompted a CT angiography of head and neck which also showed right and left internal carotid arterial dissection. Given the fact patient was on dual anti platelet agents with no neurological deficit, it was decided to continue the medical management with dual anti platelet therapy and statin.

Discussion: Hemodynamic stresses of pregnancy produce changes in arterial structure and integrity causing arterial dissection and rupture(2). The role of sex hormones like estrogen causing vasculopathy is still not known. Early detection and prompt intervention is required given high morbidity and mortality.

Ref: 1) Maeder M, Ammann P, Angehrn W, Rickli H. Idiopathic spontaneous coronary artery dissection: incidence, diagnosis and treatment. Int J Card. 2005; 101: 363-369
2) Wolff, J. Dissecting aortic aneurysm during pregnancy, parturition, and puerperium. Ned Tydschr Verlosk. 1961; 61: 23–81

3.Don't Wait- Starting Steroids in Patients with Cocaine Abuse Presenting with Respiratory Insufficiency

Mariam Abdelkader, MD, Hassan Cheema, MD*, Shubhra Ray, MD**
*York Hospital: Internal Medicine
**York Hospital: Department of Medicine, Division of Pulmonology

Introduction: Crack cocaine abuse is a poorly understood cause of both acute and chronic pulmonary toxicity which has been reported in literature on literature. It can manifest as eosinophilic pneumonia, hemorrhagic alveolitis or pneumothorax. Our case is unique as it questions the potential benefit of early steroid use in crack lung. .

Case: A 56 year-old male presented to the Emergency department with dyspnea and clinical signs of sepsis. Vital signs were significant for tachycardia, tachypnea, hypoxia and hypotension. He had bilateral decreased breath sounds with fine crackles on lung exam. CT chest revealed multifocal infiltrates with cavitation in the right upper lobe (Fig 1,2) . Empirical broad-spectrum antibiotics were started. However in less than 12 hours of admission patient was intubated for acute hypercapneic and hypoxic respiratory failure. He underwent bronchoscopy which was complicated by severe pulmonary hemorrhage resulting in emergent tracheostomy. Bronchoalveolar lavage (BAL) showed eosinophilia consistent with eosinophilic pneumonia. He subsequently developed disseminated intravascular coagulopathy with multi-organ failure. His family decided to pursue palliative extubation on Day 3 and patient expired shortly after. .

Discussion: Supportive management remains the mainstay of therapy for acute respiratory failure in addition to broad-spectrum antibiotics for crack lung. Administration of high dose steroids on admission could have had a positive impact on outcome for our patient with eosinophilic pneumonia. Waiting for BAL with eosinophilia delayed treatment in our patient. We recommend that early high dose steroids be utilized in future cases and mortality outcomes be documented to strengthen this hypothesis.

Ref. 1.) Bailey ME, Fraire AE, Greenberg SD, et al. Pulmonary histopathology in cocaine abusers. Hum Pathol 1994; 25:203.
2.) Forrester JM, Steele AW, Waldron JA, Parsons PE. Crack lung: an acute pulmonary syndrome with a spectrum of clinical and histopathologic findings. Am Rev Respir Dis 1990; 142:462

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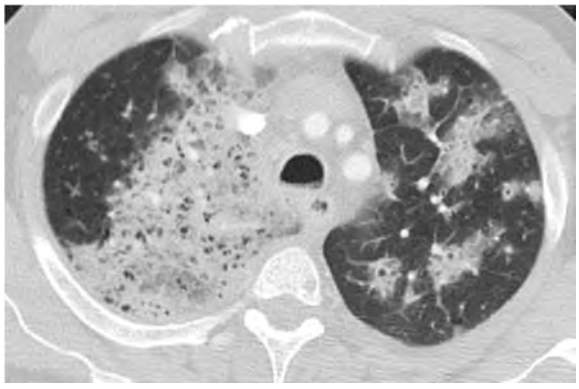

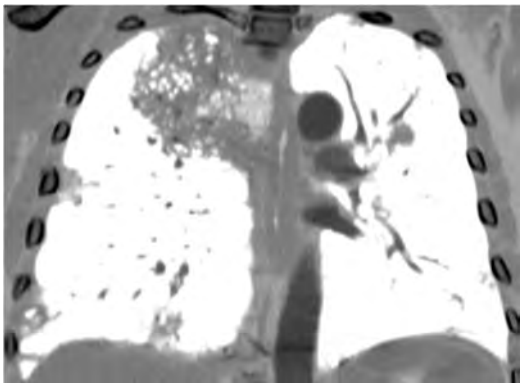

4.An Unexpected Culprit in Infective Endocarditis: *Streptococcus infantarius*

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**Easton Hospital: Department of Medicine

Introduction: We report an uncommon case of *S. infantarius* septicemia and infective endocarditis (IE) in a patient with bioprosthetic valves.

Case report: A 73 year old male with history of aortic and mitral bioprosthetic valve replacement and recently diagnosed adenocarcinoma of the colon, presented with dyspnea, fever, hypotension and leukocytosis. He was found to have a new 2/6 systolic murmur loudest at left sternal border and apex, with radiation to axilla. Septic shock was managed with broad-spectrum antibiotics and vasopressors. Two of two sets of blood cultures grew *S. infantarius*, raising suspicion of IE. Transesophageal echocardiogram (TEE) revealed a new paravalvular leak in the mitral valve prosthesis with a patent foramen ovale and a left-to-right shunt. The patient was deemed high risk for valvular surgery. Six weeks of intravenous antibiotic based on culture report was recommended. Due to advanced age and multiple comorbidities, the patient and his family members opted for oral antibiotics only.

Discussion: The Streptococcus bovis/equinus complex, which includes *S. infantarius,* was created in 2003 after an extensive taxonomic revision (1). *Unlike S. gallolyticus*, it lacks biofilm forming ability, leading to low clinical suspicion of its implication in IE (2). This could delay the diagnosis and therefore patient care. We suggest having a high clinical suspicion and low threshold for performing TEE in suspected cases. To the best of our knowledge, very few cases of S*. infantarius* IE have been reported. Growing recognition of *S. infantarius* causing fatal IE calls for further investigation regarding its pathogenesis in IE.

Ref. (1) Jans C, Meile L, Lacroix C, Stevens MJ. Genomics, evolution, and molecular epidemiology of the Streptococcus bovis/Streptococcus equinus complex (SBSEC). Infect Genet Evol. 2015;33:419.
(2) Corredoira, J., M. P. Alonso, J. García, E. Casariego, A. Coira, A. Rodríguez, J. Pita, C. Louzao, B. Pombo, M. López, and J. Varela. 2005. Clinical characteristics and significance of Streptococcus salivariusbacteremia and Streptococcus bovis bacteremia: a prospective 16-year study. Eur. J. Clin. Microbiol. Infect. Dis. 24250-253.

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5. A Rare Presentation of Pulmonary Renal Syndrome

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**Drexel University College of Medicine: Department of Medicine, Division of Internal Medicine

Introduction: Pulmonary renal syndrome (PRS) is the combination of diffuse alveolar hemorrhage and rapidly progressive glomerulonephritis. Autoimmune diseases, such as ANCA associated vasculitis (AAV) and Goodpasture's syndrome (GPS), are the most commonly implicated triggers of PRS. (1) In rare cases of AAV, concomitant GPS and preceding pulmonary fibrosis have been reported and may independently portend a poor prognosis. (2, 3) We report a case of PRS with both prognostic factors.

Case: A 54 year-old male with no pertinent past medical history presented with worsening

shortness of breath and bilateral lower extremity swelling of 1 week duration. Patient had presented approximately one-month prior with similar complaints. On that admission, CTA chest demonstrated basal and peripheral predominant honeycombing, ground glass opacities at lung bases, multiple pulmonary nodules, and bilateral pleural effusions. Patient was discharged for outpatient work-up of interstitial lung disease. Patient denied associated symptoms and no risk factors for exposure to silica, asbestos, and beryllium were found. Physical examination was remarkable for dry rales at lung bases and 2+ pitting edema bilaterally to mid shins. On lab work, creatinine was elevated to 7.33 compared to 1.08 on prior admission. Renal biopsy confirmed rapidly progressive glomerulonephritis and autoantibody screen was positive for P-ANCA and anti-GBM. Treatment was initiated with dialysis, plasma exchange, steroids, and immunosuppression.

Discussion: Clinical presentation of PRS may vary thus posing a challenge for diagnosis. A high degree of clinical suspicion is required for early detection and intervention, which has shown to increase survival and decrease morbidity.(1)

Ref. 1. West SC, Arulkumaran N, Ind PW, Pusey CD. Pulmonary-renal syndrome: a life threatening but treatable condition. Postgrad Med J. 2013 May;89(1051):274-83. doi: 10.1136/postgradmedj-2012-131416. Review. PubMed PMID: 23349383 .
2. Rutgers A, Slot M, van Paassen P, van Breda Vriesman P, Heeringa P, Tervaert JW. Coexistence of anti-glomerular basement membrane antibodies and myeloperoxidase-ANCAs in crescentic glomerulonephritis. Am J Kidney Dis. 2005 Aug;46(2):253-62. Review. PubMed PMID: 16112043.
3. Katsumata Y, Kawaguchi Y, Yamanaka H. Interstitial Lung Disease with ANCA-associated Vasculitis. Clin Med Insights Circ Respir Pulm Med. 2015 Sep 23;9(Suppl 1):51-6. doi: 10.4137/CCRPM.S23314. Review. PubMed PMID: 26448696; PubMed Central PMCID: PMC458309

6.An Unusual Cause of Abdominal Lymphadenopathy

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**Abington Memorial Hospital: Department of Pathology

Case: 29 year-old woman presented to the emergency room with 1-week of lower abdominal pain and fever. She denied nausea, vomiting, loose stools or dysuria. Past medical history included iron deficiency anemia from heavy menses, 3 cesarean sections and bilateral tubectomy. Her temperature was 104.6°F, heart rate 121/minute, respiration rate 18/minute, and blood pressure 133/68 mm Hg. She had tenderness in the right lower quadrant, without guarding or rebound. White cell count was 2900 cells/mm3. Abdominal CT revealed abnormal thickening of the appendix with periappendiceal changes and multiple enlarged right retroperitoneal and right inguinal lymph nodes. With a high clinical suspicion for acute appendicitis, a laparoscopic appendectomy with lymph node excision was done. Grossly, the appendix appeared normal, and there was minimal inflammation on histopathology. Histopathological exam of the excised inguinal node showed patchy areas of necrosis with karyorrhectic debris of histiocytes and monocytes, confirmed by immuno-histochemistry for CD68. Acid-fast staining for mycobacterium and methenamine silver staining for fungi were negative. These findings were supportive of Histiocytic Necrotizing Lymphadenopathy- also known as Kikuchi-Fujimoto disease. Serological testing for

viral diseases (HIV, EBV, CMV), bartonella and ANA were negative. The patient's abdominal pain and fever persisted for a week and then gradually resolved with supportive treatment. **Discussion**: Kikuchi-Fujimoto disease is a self-limiting condition. It is usually seen in young females and often presents with fever and tender cervical lymphadenopathy, although there have been cases reporting intra-abdominal lymphadenitis (2). Therapeutic measures are generally limited to symptomatic treatment, but some may require steroids.

Ref. 1. Ura H, Yamada N, Torii H, et al. Histiocytic necrotizing lymphadenitis (Kikuchi's disease): the necrotic appearance of the lymph node cells is caused by apoptosis. J Dermatol 1999; 26:385 .
2. Vijayaraghavan R, Chandrashekar R, Saraswathi A, Belagavi CS. Kikuchi-Fujimoto's disease involving mesenteric nodes: a report and review of literature. BMJ Case Reports 2011;10 .
3. Payne JH, Evans M, Gerrard MP. Kikuchi-Fujimoto disease: a rare but important cause of lymphadenopathy. Acta Paediatr 2003; 92:26

Abstracts-Research

1.Effect of Extreme Obesity on Medical Abortion Completion

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**Drexel University College of Medicine: Department of Obstetrics and Gynecology

OBJECTIVE: Medical abortion is a common type of abortion and accounted for 19.1% of elective terminations of pregnancy in 2011 (1). In addition, the CDC also reports that 31.8% of women aged 20-39 are obese with a BMI ≥30 and 7.7% have a BMI ≥40 (extreme or morbid obesity) (2). The goal of this study was to compare the effectiveness of elective termination of pregnancy using medical abortion between extremely obese women with a BMI≥40 and women with a BMI<40. **METHODS**: We reviewed all of the charts for women seeking medical abortion from a family planning clinic between January 2010 and April 2016 (N=99). Adult women with intrauterine pregnancies between 5 weeks 0 days and 9 weeks 6 days who took both mifepristone and misoprostol were included. The primary outcome was completion of the abortion after one dose of each drug as documented at a follow-up visit. . **RESULTS**: In the BMI<40 group (n=95) 91% of patients completed their medical abortion, 6% did not and needed additional medication or a procedure to complete their abortion. Three percent were lost to follow-up. In the morbidly obese group, BMI≥40, (n=4) one patient needed a dilation & evacuation procedure to complete her abortion and the other 3 had successful medical terminations of pregnancy. **DISCUSSION**: This data suggests there may be a lower rate of medical abortion completion in extremely obese women, however no statistically significant difference could be determined due to small sample size. Further study is needed to answer this clinically

important question. .

Ref. 1. K. Pazol, A. Creanga, K. Burley, D. Jamieson. MMWR: Abortion Surveillance—United States, 2011. Surveillance Summaries. Nov 28, 2014. 63(SS11);1-41. cdc.gov
2. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of Childhood and Adult Obesity in the United States, 2011-2012. JAMA. 2014;311(8):806-814.

2.Vaginal Paravaginal Repairs: Assessment of Complication and Outcomes

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*Drexel University College of Medicine: Female Pelvic Medicine and Reconstructive Surgery
**Drexel University College of Medicine: Department of Obstetrics and Gynecology

Objective: The primary objective of this study is to describe intraoperative and postoperative complications of paravaginal defect repair. The secondary aim is to evaluate objective and subjective prolapse outcomes.

Method: This retrospective cohort included women with symptomatic stage 2-4 cystocele who underwent native tissue, vaginal paravaginal defect repair (CPT code 57285) from 2013-2015. Inpatient and outpatient

Result: A total of 129 women were included with a total of 345 concomitant procedures performed. Mean intraoperative blood loss was 119±99 mL. Two patients (1.6%) had a cystotomy and 2 (2.3%) had ureteral kinking. Three (2.3%) patients had transfusion postoperatively and 2 (1.6%) patients had hematomas that were conservatively managed. No infectious morbidity other than symptomatic vaginitis was treated, and there were no significant cardiopulmonary or thromboembolic events. Of the women who completed preoperative and postoperative questionnaires, all PFDI domains were statistically improved postoperatively. In response to the PGI-I, 20 (57%) women reported “1” as very much better and 13 (37%) reported “2” as much better. POP-Q point Ba electronic medical records were reviewed. Demographics, intraoperative and postoperative complications and pelvic organ prolapse quantification (POP-Q) measurements were obtained. Preoperative and postoperative Pelvic Floor Distress Inventory (PFDI) questionnaires and postoperative Patient Global Impression of Improvement (PGI-I) scores were evaluated. Descriptive statistics and student t-tests were used for data analysis. improved from a mean of +2.1±2.8 to -2.7±0.59. Four (3.1%) patients met criteria for anterior failure at 3 months.

Conclusion: Vaginal paravaginal repair appears to be safe procedure for repair of anterior vaginal defects.

Ref: 1. Elkins TE, Chesson RR, Videla F et al. Transvaginal paravaginal repair. A useful adjunctive procedure at pelvic relaxation surgery. J Pelvic Surg. 2000; 6:11–15.
2. Maher C, Baessler K. Surgical management of anterior vaginal wall prolapse: an evidence based literature review. Int Urogynecol J. 2006; 17:195-201.
3. Nguyen JN, Burchette RJ. Outcome after anterior vaginal prolapse repair: a randomized controlled trial. Obstet Gynecol. 2008; 111(4):891-898.
4. White GR. An anatomic operation for the cure of cystocele. Am J Obstet Dis Women Child. 1912; 65:286–290.
5. Arenholt LTS, Pedersen BG, Glavind K et al. Paravaginal defect: anatomy, clinical findings, and imaging. Int Urogynecol J. 2016. Epub ahead of print.

3.Identifying Genetic Biomarkers of Ovarian Reserve in Women

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**Drexel University College of Medicine: Department of Microbiology and Immunology
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BACKGROUND: In women, the number and quality of oocytes, collectively called "ovarian reserve", and the gradual decrease of these parameters with age, largely determines reproductive potential1. Current tests of ovarian reserve are limited and do not predict the likelihood of pregnancy or live birth2. Previously we identified *Chtf18*, a regulator of mammalian meiosis3. We demonstrated that *Chtf18*-null female mice exhibit a phenotype which closely resembles that of women with diminished ovarian reserve. Our work suggests a role for *Chtf18* (*CHTF18* in humans) and cohesins in female fertility and ovarian reserve. Thus, our objective is to identify new and improved biomarkers of ovarian reserve in women.
METHODS: A bioinformatics approach was used to identify a biochemical pathway of genes functionally related to *CHTF18*. Next generation sequencing will be utilized to identify genetic variants that correlate with diminished ovarian reserve in women.
RESULTS: Currently, women aged 30-45, comprising 3 groups of 96 each, are being enrolled in our study. Blood samples have been collected and DNA purified from 36 infertile women with diminished ovarian reserve (experimental group) and 87 infertile women with normal ovarian reserve (control group). Women with proven fertility (second control group) will soon be enrolled. Purified DNA is being processed and will soon be sequenced.
CONCLUSIONS: Genetic variants of *CHTF18* and genes functionally related including cohesins, may be biomarkers of ovarian reserve.
DISCUSSION: Information gleaned from our study could identify women at risk for diminished ovarian reserve later in life, and allow them to make earlier reproductive choices.

Ref. 1. Broekmans, F.J., Soules, M.R., and Fauser, B.C. Ovarian aging: mechanisms and clinical consequences. Endocr Rev 30, 465-493 (2009.)
2. American College of Obstetricians and Gynecologists, Committee Opinion no. 618: Ovarian reserve testing. Obstet Gynecol 125, 268-273 (2015.)
3. Berkowitz, K.M. et al. Disruption of Chtf18 causes defective meiotic recombination in male mice. PLoS Genet 8, e1002996 (2012.)

4.Considering mode of infection when caring for the pregnant HIV+ population

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**Drexel University College of Medicine: Department of Medicine, Division of Infectious Diseases and HIV Medicine
***Drexel University College of Medicine: Department of Obstetrics and Gynecology

OBJECTIVE: To assess whether mode of infection affects maternal and fetal pregnancy outcomes when analyzing perinatally infected versus behaviorally infected HIV+ patients.
METHODS: A retrospective chart review was conducted assessing patients seeking care at Drexel's HIV clinic from February 2000 to August 2015. Information collected included

demographics, maternal and fetal outcomes were assessed by viral load (VL) and CD4 count, as well as fetal birth weight, gestational age and HIV status when delivered. Subjects were divided between mode of infection: perinatal versus behavioral. .

RESULTS: The charts of 324 behaviorally infected and 14 perinatally infected pregnant patients were reviewed. Of the demographics, only mean age was significantly different (20.9 in the perinatal vs. 28.0 in the behavioral, p 0.006). Absolute CD4 count was higher in behaviorally infected patients. At the start of pregnancy, 41.7% perinatally infected patients had CD4 <200 at the compared to 15.3% of behaviorally infected. Viral load (VL) also significantly differed (p 0.007) between the two populations. At delivery, 86% of behaviorally infected patients had a VL<1000 vs 67% of perinatally infected (p 0.05). However, when evaluating for fetal outcomes at birth, including weight, gestational age and HIV status, there was no significant difference between the two groups.

DISCUSSION: Overall, the perinatally infected population had higher VL and lower CD4 counts throughout pregnancy. This could to be linked to increased multidrug resistance due to poor drug adherence and multiple psychosocial factors including stigma of being born with HIV. However, despite this, there was no difference in fetal outcomes.

Ref. 1. MacDonell, K. et al. "Barriers to Medication Adherence in Behaviorally and Perinatally Infected Youth Living with HIV." AIDS and behavior 17.1 (2013): 86–93. PMC.
2. Morbidity and Mortality Weekly Report, Vol. 55, No. 21 (June 2, 2006), pp. 592-597
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5.Urodynamic Testing is Not a Reliable Predictor of Pathology Between Hunner Lesion(s) and Mucosal Cracks

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**Drexel University College of Medicine: Department of Obstetrics and Gynecology

Objective: To determine the similarities and differences on urodynamic testing between interstitial cystitis (IC) patients with Hunner lesions and IC patients with mucosal cracks.

Methods: Eighty-five women with the diagnosis of IC at a single tertiary center. Patients had urodynamic studies (UDS) followed by cystoscopy and bladder hydrodistention between January, 2011 and July, 2014. Patients were assessed using daily pain on pre-operative visual analog score (VASD), pain during sex (VASS), the IC symptom index (ICSI), IC problem index (ICPI) and the female sexual function index-19 (FSFI-19). The pre-operative UDS were reviewed for post void residual (PVR), maximum functional bladder capacity, incontinence on urodynamic testing, pelvic floor dysfunction (PFD) on electromyography (EMG), pain during testing, detrusor overactivity (DO), and bladder outlet obstruction (BOO). The operative reports were reviewed for bladder pathology, and maximum anatomical capacity.

Results: In total, thirty-three women had a Hunner lesion and 52 women had a mucosal crack on cystoscopy. The questionnaires were compared between the two groups, VASD (p=0.23), VASS (p=0.05), ICSI (p=0.8), ICPI (p=0.6) and the FSFI (p=0.01). The PVR (p=0.3),

maximum functional bladder capacity, (p=0.6) and maximum anatomic bladder capacity between the two groups (p=0.3) were not significant. The incontinence episodes between the study groups, 0.5 (p=0.9) was not significant. The results for PFD, 2.3 (p=0.1), pain, 0.01 (p=0.9), and DO, 2.7 (p=0.1) were also similar between the two groups. **Conclusions**: There is no significant difference on urodynamic testing between patients who have Hunner lesions and those with bladder mucosal cracks.

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6.The Effects of Bilateral Sacral Neuromodulation in Interstitial Cystitis Patients

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BACKGROUND: Interstitial cystitis/bladder pain syndrome (IC/BPS) is defined as an unpleasant sensation perceived to be related to the urinary bladder associated with lower urinary tract symptoms. The objective of this study is to examine the changes in urinary and pain symptoms and anesthetic bladder capacities of patients after unilateral and bilateral SNM. **METHODS**: This is a retrospective study of patients with IC/BPS treated with unilateral SNM and subsequent bilateral SNM at a tertiary care center. Patient responses on visual analog scales (VAS) for pain with daily activities, frequency, urgency, nocturia and anesthetic bladder capacities at baseline and post bilateral implant were recorded. Demographic statistics, student t-tests and chi-squared analyses were used.

RESULTS: Thirty-two patients were identified and mean age of the study population was 51. There were statistically significant changes in VAS scores in baseline visit to post-unilateral placement comparison (p=0.002), baseline visit to post-bilateral placement (p=0.002), and baseline to 1-year post-bilateral placement follow up (p=0.01). Comparison of baseline to post-unilateral and post-bilateral placement revealed significant changes for nocturia (p=0.005, p=0.0002), frequency (p=0.01, p=0.0006), and VAS scores (p=0.002, p=0.002). Nine patients out of 32 had an average anesthetic bladder baseline capacity of

777mL.The overall anesthetic bladder capacity after bilateral placement increased by 55mL (p=0.65).

CONCLUSIONS: Sacral neuromodulation is an effective treatment for the symptoms of IC/BPS including urgency, frequency and pain. There is a mild increase in capacity but limited to patients who had repeat hydrodistention post bilateral placement and may not be reflective of the IC/BPS population.

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7. Demographic Factors Influencing the Time Interval to Hysterectomy in the Treatment of Symptomatic Uterine Fibroids

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Introduction: While fibroids are the most common indication for hysterectomy current guidelines support uterine-conserving therapy. The relationship between demographic factors and clinical characteristics in women who undergo a hysterectomy has not been well established.

Objectives: The primary objective of this study was to investigate clinical characteristics associated with a shorter time interval to hysterectomy.

Results: A total of eighty-seven women aged thirty-two and fifty years were included. The mean time to hysterectomy was 2.5 years from initial presentation with 55% of women undergoing a hysterectomy at 2 years after initial presentation. Women with Medicaid insurance had a shorter time interval to hysterectomy compared to privately insured patients (p=0.03). Age at initial presentation (R = -0.529; $p < 0.001$) and symptom onset (R = -0.22; p = 0.044) also correlated with a shorter time interval to hysterectomy. Other demographics assessed do not correlate significantly with the time interval to hysterectomy.

Conclusion: Further investigation is needed to determine the relationship between insurance status and the shorter time interval leading to hysterectomy. Larger comparative studies need to be performed before recommending hysterectomy as a first line treatment for patients based on demographic or clinical factors.

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8.Physician Delivery Volume: Impact on Prime Cesarean Delivery Rate

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Objective: Evaluate the relationship between provider delivery volume and prime cesarean rate.

Methods: The Statewide Planning and Research Cooperative System for New York(SPARCS) maintains data for all discharges. This database was utilized to identify 33 hospitals that did not utilize midwives. Data from hospitals utilizing midwives was excluded to eliminate confounding. For each hospital, the number of deliveries and number of delivering physicians was determined utilizing SPARCS data. The prime cesarean rate for each hospital was obtained from the New York State Department of Health. Average delivery volume per delivering physician was calculated for each hospital. A Pearson correlation coefficient was calculated to determine the correlation between physician delivery volume and prime cesarean

Results: The thirty-three hospitals had delivery volumes from 190 to 6,179. Average delivery volume per facility was 908. Average delivery volume per physician for each facility ranged from 21 to 144. The Pearson correlation coefficient for physician delivery volume and prime cesarean rate was 0.33 with a p value of 0.065.

Conclusion: The data indicate that a modest positive correlation exists. A p value of 0.05 is used to indicate statistical significance. Utilizing this threshold, the p value for the Pearson coefficient is not statistically significant. While this study does not demonstrate a statistically significant correlation, physician work load and the impact it may have on patient care deserves consideration as workload is projected to increase. Further study is crucial to ensuring strategies are employed to meet the challenges that we will face in coming year.

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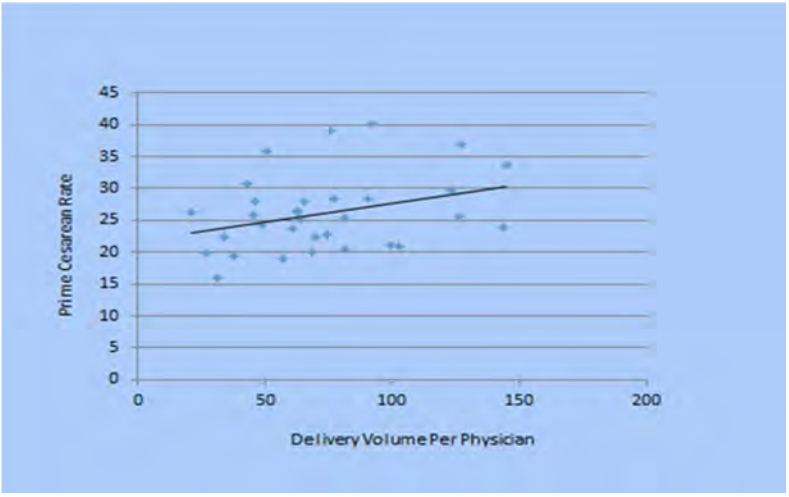

Fig 1 Correlation between provider delivery volume and Prime Cesarean rate.

9.Utility of Intracardiac Echocardiography in Evaluating Pacemaker and ICD Lead Infections and in Identifying Complications Post Extraction: A Single Center Experience

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***Drexel University College of Medicine: Clinical Cardiac Electrophysiology
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Introduction: With increasing prevalence of cardiac comorbidities there is greater need for pacemaker and ICD implantation. As a result, the incidence of infection, lead malfunction and need for device upgrades have also increased.
Objective: To describe our experience with ICE during device lead extraction and to assess its sensitivity in detecting vegetations.
Methods: Single center extraction records were reviewed from 2004-2016 in patients who underwent pacemaker/ICD extractions.
Results: ICE was used in 470 extraction procedures; indications included infection (348), lead malfunction (101), upgrades (10), and Other (11). ICE identified vegetations in 157 patients: tricuspid valve (34), device leads (115), right atrial (RA)/superior vena cavae (SVC) junction (3), inferior vena cavae (IVC)/RA junction (1), aortic valve (3), eustachian valve (1), RA wall (2). Of the infection related extractions, 113 additionally had pre-operative TEE. TEE missed 11 vegetations that were picked up by ICE imaging. Vegetation location seen on ICE matched what was seen on TEE in 88 of the 113 cases. Major complications during extraction occurred in 16 patients and included Coronary Sinus dissection/perforation (2), RV perforation (2), tamponade (5), SVC hematoma/perforation (3), IVC tear (1), Innominate Vein perforation (1), embolization of vegetation (1), flail tricuspid leaflet (1). ICE imaging was able to pickup rapidly expanding pericardial effusions and tamponade in these cases, allowing for rapid intervention. There were no complications associated with use of the ICE probe.
Conclusion: ICE is a safe and valuable tool that allows for the identification of vegetations and rapid identification of procedural complications.

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10.Mean Platelet Volume In Patients With Chest Pain

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Introduction: Chest pain accounts for about 6 million emergency department visits annually; however, only a fraction of patients who present with chest pain are found to have acute

coronary syndrome (ACS). We sought to determine whether MPV is elevated in patients who present with chest pain and are found to have ACS in our home institution to see if the parameter can be used to help risk stratify these patients. .

Methods: Patients with chest pain who were admitted to Hahnemann University Hospital between 1/1/2010 and 12/31/2014 were stratified into non-ACS and ACS arms. A total of 397 patients were included in the study, 200 in the ACS arm and 197 in the non-ACS arm. Patients in each arm were further stratified by the following risk assessment scores: TIMI, GRACE, and EDACS scores. The study was approved by the internal review boards of both Drexel University College of Medicine and Hahnemann University Hospital.

Results: We found that MPV in the ACS group was significantly higher in the ACS arm (8.9 ± 1.1 fL vs. 8.6 ± 1.2 fL, p = 0.006, with error reported as one standard deviation). Elevated MPV was found to be an independent predictor of ACS regardless of risk assessment score. Conclusion: MPV is significantly elevated in patients who present with chest pain and are found to have ACS compared to patients who are not found to have ACS, even in patients with similar risk assessment scores.

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11.Simulation- The Future is Here

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**Monmouth Medical Center: Department of Medicine

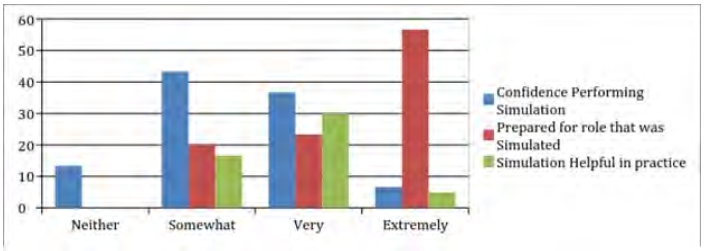
Introduction: The education of health care providers is an integral part of patient safety. Both virtual patients and technology-enhanced simulation are consistently associated with large, statistically significant benefits in the areas of knowledge, skills and behaviors. For direct patient effects (e.g., major complications, mortality, or length of stay), the benefits are smaller but still significant.1,2

Objective: To assess differences in outcome with simulation training. .

Methods: Our facilities at Monmouth Medical Center include a SimMan, a SimMan 3G, and multiple task trainers that are routinely used for simulating specific tasks. As phase 2 of the study, we performed a cross-sectional study using a simple 10-point questionnaire to assess self-reported improvement in performing tasks related to simulation activities.

Results: 74% of respondents were Nurses and 19% Medical Residents. 76% felt that practice would help them improve their confidence; 46% felt that simulation would be beneficial. 55% of respondents have participated in simulation and 90% of them felt their performance improved after the simulation. 43% felt confident performing tasks involved with simulation. 56% felt that they were better prepared for the simulated tasks. Simulating a specific task made more than 90% of respondents who had simulation experience feel more confident and better prepared and it was requested as one of the ways to improve their professional role by around 50% of total

respondents. From the responses, simulation based education is effective and asked for. It provides a low risk skill rehearsal with repetitive and structured practice in addition to the assessment and feedback.



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12.A positive trend in reducing the inpatient burden of nonspecific chest pain: An Analysis of the National Trend in the United States from 2006 to 2012

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Objective: Chest pain is one of the most common complaints for which a patient visits the hospital [1]. PURSUIT, TIMI, GRACE, FRISC and HEART are scoring systems used to evaluate the severity and the need for admission of these patients. [2] The aim of this study was to evaluate emergency department(ED) visit rates, inpatient admission rates, demographics and cost related to nonspecific chest pain from 2006 to 2012.

Methods: We analyzed data from the National Inpatient Sample Database(NIS) for all patients in which nonspecific chest pain (ICD-9 code 786.5) was the principal diagnosis from 2006 to 2012. Spearman's coefficient was utilized for statistical analysis, which was computed using SASv9.3.

Results: During 2006 to 2012, the linear trend of ED visits for nonspecific chest pain has increased from 3,736,502 to 4,646,074 (rho=1,p<.0001), whereas the number of admissions to the hospital has decreased from 709,964 to 438,026 (rho= -0.964,p=0.0005). While the mean length of stay remains the same as 1.8 days, the mean charges per hospital discharge have increased from $15,027.25 (adjusted for inflation) to $21,057 (rho=1,p<.0001). The age group 45 to 64 years constitute for most of the admission.

Discussion: Though there has been an increase in the number of patients who visit the ED for nonspecific chest pain, there has been a positive trend in the reduction of admissions for the same. This can be attributed to the increase in usage of scoring systems. Further reduction in diagnostic procedures is needed to reduced mean charges per hospital discharge.

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Articles

1.Management of Ruptured Appendix in Pregnancy: A Novel Approach

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**Monmouth Medical Center: Department of Ob/Gyn

Case: Our case is a 35-year-old G3P1011 female at 34 weeks and 2 days gestation who was transferred to our facility from a nearby hospital for suspected appendicitis in pregnancy. She presented initially with complaints of abdominal pain and subjective fever. She also reported anorexia and nausea for 11 days. The pain was initially peri-umbilical in nature radiating to her right side. She had no obstetrical complaints. Her pregnancy was also complicated by advanced maternal age, hypothyroidism, and a history of a previous Cesarean for gestational hypertension and diabetes. An ultrasound was performed at the prior facility which could not visualize the appendix. An MRI was then performed which found a fluid collection in the right lower quadrant.

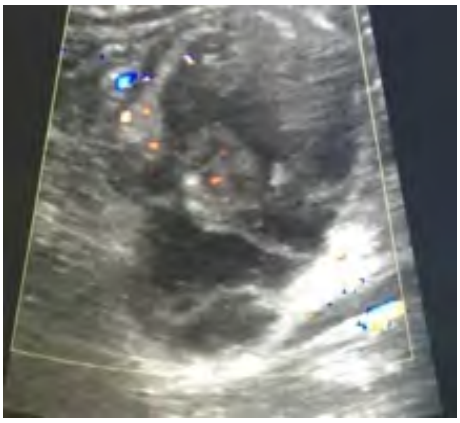

Fig 1.

Physical exam on admission revealed focal right lower quadrant tenderness with no guarding or rebound tenderness. Psoas and Rovsing's sign were both negative. She had a mild tachycardia of 107 /min and a temperature of 99.7 degrees Farenheit. Fetal status was reassuring. The laboratory work was significant for white blood cell count of 17200 with bands of 2. The patient was started on broad spectrum antibiotics. A repeat ultrasound done at our hospital showed a 7 .5x 5.1x 4.5cm complex fluid collection in right lower quadrant (Fig 1) which was not present on the previous study.

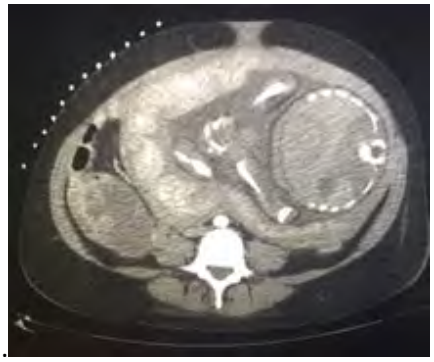

Fig 2

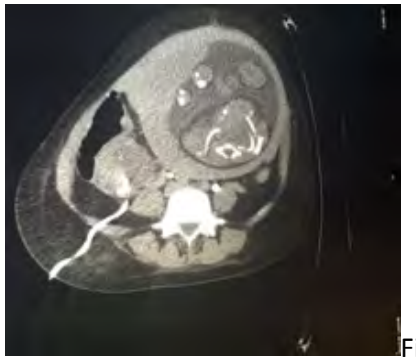

Fig 3

As per recommendation of maternal and fetal medicine (MFM) specialist and surgical team, percutaneous drainage of the appendiceal abscess by interventional radiology (IR)

was performed. A percutaneous pigtail drain was placed under CT guidance by IR and green purulent fluid was drained (Fig 2&3 below).As per Infectious Disease consultant's recommendation, Vancomycin was also added to cover the gram-positive cocci, which was detected by the Gram stain of the purulent fluid drained. After the procedure, patient improved and she was discharged on hospital day five. A CT scan of abdomen and pelvis was repeated 4 days later which showed decrease in the size of the abscess to 3.6cm×3.7cm. Fetal status remained reassuring throughout. Finally, the patient had an elective low transverse cesarean section at 39 weeks' gestation with delivery of a viable neonate. Intra-operative evaluation of the right lower quadrant revealed intra-abdominal adhesions and walled-off phlegmon which were left in-situ. The percutaneous drain was removed on postpartum day one. A fistulogram (Fig 4) was performed prior to removal of the drain which showed no collection or cavity upon contrast injection. .

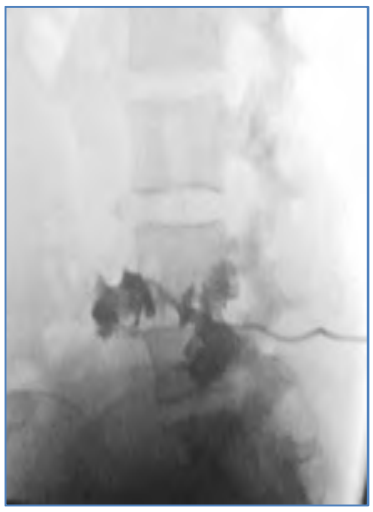

Fig 4

Her postpartum recovery was uneventful and she was discharged in a stable condition on postpartum day 3. The patient is currently doing well and has been asymptomatic till this date and has not needed an appendectomy thus far.

Discussion: Acute appendicitis is suspected in 1/600 to 1/1000 pregnancies and it is considered the most common surgical emergency in the pregnancy. The diagnosis of appendicitis during pregnancy is challenging secondary to anatomical changes of pregnancy, physiologic leukocytosis and variety of abdominal discomforts that are common during pregnancy. As a result, appendiceal perforation tends to occur more frequently during pregnancy which poses a significant maternal and fetal morbidity. Prompt appendectomy is the most common treatment for uncomplicated appendicitis.(1) A perforated appendix is the leading surgical cause of fetal loss during pregnancy.(2) The intraabdominal infection can lead to peritonitis, sepsis, preterm labor, and fetal loss.(2,3) Ruptured appendicitis remains a major predictor of fetal loss; McGory et al(4) found the rate of fetal loss was three times that with simple appendicitis. In their 1977 case review of 300 pregnant patients with appendicitis, Babaknia et al(5) found that the rate of fetal loss with non-perforated appendicitis was 1.5% compared with the rate of fetal loss with perforated appendicitis of 35.7%. Preterm labor and delivery is common in women with perforated appendicitis(4) due to the intraabdominal inflammatory response. Despite the fact that there is extensive data about the appendiceal perforations in the non-pregnant population, there is limited data available in the pregnant population. In a study by Young et al(6), two pregnant patients with walled-off appendiceal perforations were initially treated medically with antibiotics IV fluids and bowel rest. The first patient had a successful vaginal delivery but had a

subsequent appendectomy two months postpartum. The second patient was also treated medically on initial presentation but she then had an appendectomy during a cesarean delivery for breech presentation in preterm labor. In another study, only one out of 38 patients was treated conservatively with increased evidence of complications.(7) In our case, the patient was transferred to our facility with a walled off appendiceal abscess as a result of a ruptured appendix with pregnancy and decision was made to treat the patient conservatively with antibiotics and IR drainage. Patient responded well to this intervention and she was able to carry the pregnancy to term and delivered by elective cesarean section. In comparison to most established data and case reports, this approach eliminated the need for surgical intervention in pregnancy and other possible morbidities associated with it. In contrast to the previous cited cases, our patient did not need any surgical intervention up until this point.

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2.Vulvar Edema in the Setting of Preeclampsia: A case of conservative management

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**Monmouth Medical Center: Department of Ob/Gyn

Introduction: Although not considered diagnostic criteria for preeclampsia, edema may be present in severe cases due to fluid retention and accumulation of extracellular fluid secondary to endothelial injury (1). Rarely, edema may be confined to the vulvar region. Several case reports of severe vulvar edema in preeclampsia have been noted in the literature (2,3,4,5). It may represent a predictor of advancement to severe preeclampsia (6). Few treatment approaches have been suggested (2,3,4). We present a severe case of vulvar edema at Monmouth Medical Center, which was treated conservatively with topical therapy until 32.3 weeks of gestational age (wga).

Patient is a 30 year old G2P0010 at 29.0wga with dichorionic-diamniotic pregnancy admitted with preeclampsia without severe features. Her physical exam was most notable for elevated blood pressures and 4+ lower extremity edema extending to the knees. She received magnesium therapy for fetal neuroprotection as well as steroids for fetal lung maturity. On hospital day number three the patient began to exhibit signs of severe vulvar edema with no

evidence of necrosis (Figure 1). For two weeks, supportive care of the vulva was maintained with application of Vaseline and topical benzocaine spray. Weeping was noted without tissue breakdown. At 32.3wga, the patient underwent a cesarean section secondary to worsening preeclampsia. Immediately post-operatively the vulvar edema reduced by fifty percent. At her post partum visit several weeks later, vulva had completely returned to baseline (Figure 2).

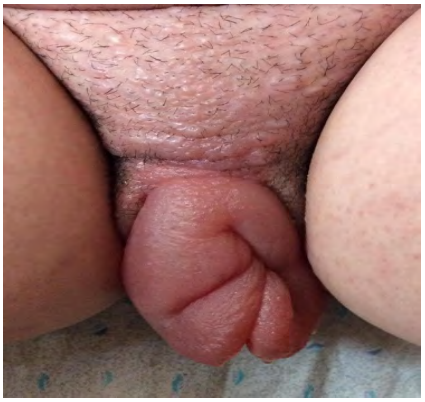

Figure 1: Severe vulvar edema at 30wga associated with pre-eclampsia

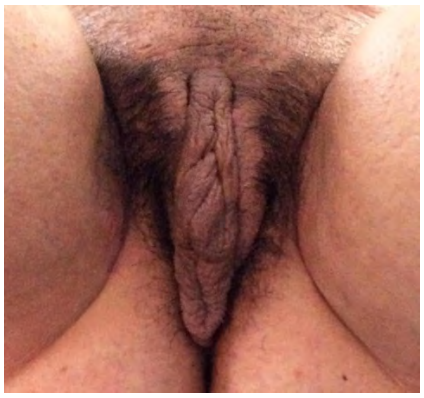

Figure 2: Post partum resolution of vulvar edema

Discussion: Vulvar edema is incredibly uncomfortable for the patient and may become a deciding factor in timing of delivery. Although rare, a variety of options for symptomatic relief have been noted in the literature. Water submersion hydrotherapy has been shown to shift interstitial edema back into the vascular space and relieve edema (2). Another study demonstrated improvement with manual techniques that encourage lymphatic drainage (3). Direct drainage of vulvar edema by needle puncture was shown to be effective in a report of vulvar edema in preeclampsia at 35wga (4). A topical treatment approach was described in this case. This, combined with close monitoring for progression to severe preeclampsia, was effective in prolonging the pregnancy until severe preeclampsia developed at 32.3wga without long-term vulvar sequelae. Conservative treatment approaches are important considerations for symptomatic relief of vulvar edema until medically indicated delivery occurs.

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3.Three Cases of the Unwanted Tetrad - A Case Series on Human Babesia

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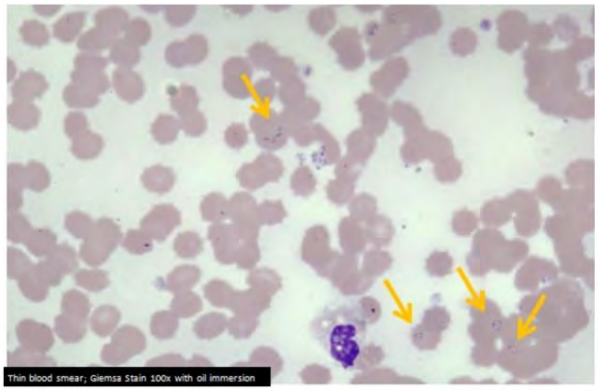
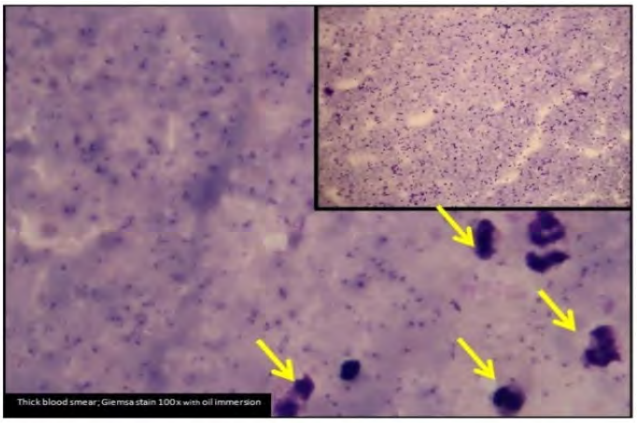
Introduction.: This case series describes 3 human infections with Babesia species treated at our hospital in the summer of 2016. Babeiosis is a zoonotic disease that requires both a vertebrate reservoir and an invertebrate vector for successful transmission.1In the United States, most cases of human babesiosis occurs in the coastal north-eastern regions and infections are usually caused by Babesia microti. Although some cases of babesia acquired through blood transfusion have been described,2 infection mostly frequently occurs during blood meals of infected ticks of the genus I. xodes.3 I. scapularis can feed on both infected white-tailed deer and white-footed mice and subsequently transmits Babesia microti to humans. I. scapulars is also the vector for the bacteria that cause Lyme disease and human granulocytic ehrlichiosis (Borrelia Burgdoferi and Ehrlichia chaffeensis).4 The life cycle of I. scapularis has the larva, nymph and adult stages of development, it takes two years for completion.1 The nymphal tick is the primary vector for transmission of B. microti to humans even though larvae and adult ticks also feed on humans.5 Cases of babesiosis typically increase in the warmer months because during these months ticks and humans more frequently can be found active in the same environment. The small size of the nymph (<2.5mm), its pale grey ground color, inconspicuous feeding site and benign local reaction to blood feeding make recollection of nymphal tick bite a rear finding.5 Prompt careful removal of the tick can reduce the chances of infection because transmission peaks as the tick reaches complete engorgement with the hosts blood. Babesiosis caused by B. divergens occurs mostly in asplenic patients where it is typically fulminant and hemolytic.3 In contast, B. Microti frequently leads to sub-clinical or mild infections, however clinical infections are more likely in asplenic patients, patients with concurrent Lyme disease in endemic areas, immunosuppressed individuals and elderly people with comorbidities.6 Symptoms of the disease may sometimes be life threatening, but it s rarely fatal. Symptoms of B. microti appear 1-4 weeks after the bite.7 Onset is gradual, common symptoms are: malaise, fatigue, anorexia shaking and chills. Subsequently, intermittent or sustained fevers occur within a week.8 Also mild hepatomegaly and splenomegaly may occur, but not lymphadenopathy.

Babesiosis is usually diagnosed by microscopic examination of Geimsa stained thin blood smears. Babesia species appear annular, oval or piriform.9 The ring form which is commonly seen strongly resembles the ring form of Plasmodium falciparum. The following features distinguish it from P. falciparum- Occasional merozoites arranged in tetrads, referred to as "Maltese Cross", Occasional exoerythrocytic parasites (when parasitemia is high), Absence of brownish pigment deposits (hemozoin) in ring forms and absence of gametocytes.10 Typical

laboratory findings include: hemolytic anemia, lowered levels of serum haptoglobin, elevated reticulocyte counts and a percentage of infected erythrocytes ranging form 1%-10% in people with intact spleens but may be as high as 85% in the aspleenic group.1 Other lab findings may include elevated erythrocyte sedimentation rate, a positive direct Coomb's test, proteinuria, hemoglobinuria, elevated liver enzymes and elevation of creatinine and blood urea nitrogen.11 Patients with B. microti infections tend to have a mild illness and recover without chemotherapeutic interventions. However, in patients with severe infections combination therapy with clindamycin (300-600mg every 6hours intravenously or intramuscularly) and oral quinine (650mg every 6-8 hours) taken for 7-10 days is usually effective. In patients with the milder form to the disease, oral clindamycin 600mg every 8 hours given with oral quinine may be used for a week. An alternative regimen is using the combination of atovaquone with azithromycin. The dose of azithromycin is 500mg on the first day and 250mg daily thereafter; the dose of atovaquone in adults is 750 orally taken twice daily for 7-10 days.12



Thin smear with arrows showing multiple infected red blood cells containing Babesia sp. Trophozoites. Some red blood cells containing multiple ring forms.



Thick blood film the blood is concentrated in a small area that is many cell layers thick. During staining the erythrocytes dehemoglobinize and only leukocyte nuclei [yellow arrows], platelets and parasites [small dots in background] are visible.

Inset image is taken at x4.

Table 1. Key Features of the 3 Cases in this series.

	Case 1	Case 2	Case 3
Age (years)	68	65	71
Sex	Male	Male	Male
Residence	PA	PA	PA
Recent travel history	NJ	NY, MI	DE
Presenting complaints	Fever, fatigue, anorexia	Fever	Fever, chills, nausea, myalgia, jaundice
Initial % parasitemia	4	3	12
Presence of immunocompression	No	No	No
Hemoglobin at presentation (g/dL)	10.6	11.7	9.6
Hemoglobin nadir	6.4	9.2	8.0
Platelet count at presentation (x 10^9/L)	56	68	36
Complications	Severe anemia, respiratory failure	-	Hypotension, severe anemia, AKI
Pharmacological therapy	Clin+Quin, Doxy	Clin.+Quin. /Atov.+Azith, Doxy	Clin+Quin, Doxy
Days spent on admission	19	6	12

Notes: PA=Pennsylvania; NJ= New Jersey; NY=New York; MI = Michigan; DE= Delaware; N/A= Not Available; AKI= Acute Kidney Injury; Clin= Clindamycin; Quin = Quininie ; Doxy= Doxycycline ; Atov= Atovaquone ; Azith = Azithromycin

Case 1: In June 2016, a 68 year old man presented to the emergency department (ED) with complaints of fever with associated rigors and chills, fatigue and a decreased appetite all of about 2 weeks duration. He also reported previously noticing a large rash on his distal part of his left leg while at Jersey shore about 4 weeks prior to presentation. He resides in Pennsylvania. At the ED he was noted to become hypotensive .Physical exam was significant only for fever, chest x-ray revealed some increased densities in the Left lingula suggestive of pneumonia. Lab findings were significant for reduced white blood cell count of 3.3×109/L and lactic acid of 3.4mEq/L. and had markedly elevated liver enzymes and total bilirubin levels, his Hemoglobin (Hgb) was 10.6 g/dL and platelets were 56x 109/L. Due to the history of a recent lower extremity rash, thick born diseases were a part of the differentials. Further work up revealed positive IgM for Lyme disease, in addition intra-erythrocytic parasites very suggestive of Babesia were seen in blood smear with a 4% parasitemia, serologies for ehrlichia and anaplasma returned negative. Haptoglobin was <8mg/dL, Lactate dehydrogenase (LDH) and reticulocyte counts were elevated. Blood and urine cultures were not contributory. The patient was started on oral quinine 648mg Q8, intravenous (IV) clindamycin 600mg Q 8 and IV 100mg bid doxycycline. He required transfusion with 2 units of packed red cells on the second day of admission because his Hgb dropped to 6.4 g/dL. Pre-transfusion percentage parasitemia was 2% paradoxically, percentage parasitemia went up to 4% day one post transfusion but subsequently consistently trended downwards thereafter. Post-transfusion, the patient developed progressive respiratory distress and

eventually required high flow oxygen via nasal canula. Chest x-ray showed pulmonary congestion/effusion this was thought to be secondary to non-cardiogenic pulmonary edema. He was subsequently upgraded form the progressive care unit to the medical intensive care unit (MICU) where he was commenced on bi-level positive airway pressure ventilation. The patient's Hgb still followed a downward trend. HgB day 1 post-transfusion was 9.3 g/L and fell to 7.0 g/L on day 3 post-transfusion. He was further transfused with 2 more units of packed red cells. Patient continued having significant hypoxic respiratory distress eventually requiring intubation with mechanical ventilation. Extubation occurred 3 days later with the patient improving clinically thereafter. He was later transferred to the general medical floors and eventually discharged to a Skilled Nursing Facility after spending 19 days on admission. The patient completed a total of 14 day antibiotic treatment for babesia along with a 14 days doxycycline therapy for concurrent Lyme disease.

Case 2: In early July 2016, a 65 year old man came to the emergency department with the main complain of fever. This was first noted about 2 weeks prior to presentation, were high grade, intermittent with associated chills. He resided a wooded area of Pennsylvania but did not recall any tick bites. Travel history included a trip to Detroit and New York both within a month prior to the ED visit. Patient had not participated in any recent significant outdoor activities. Furthermore, he had not travelled outside the country in several years. He was generally healthy apart from a past medical history of asthma. Physical exam was significant only for findings of fever with associated shivering. Other vital signs were within normal limits. Laboratory work up revealed thrombocytopenia with platelet count of 68 ×109/L, Hgb of 11.7 g/dL, haptoglobin levels were <8 mg/dL, LDH of 596U/L, reticulocytosis, Total bilirubin of 1.4 mg/dL and mildly elevated liver enzymes. Blood urea nitrogen (BUN) and creatinine were normal. Parasites were incidentally noted during the complete blood count and a 3% parasitemia was reported. A working diagnosis of babesiosis was made. Investigative work up for other thick borne infections like borrelia and anaplasma all returned negative. Blood cultures also showed no growth.The patient was given a onetime dose of 600mg IV infusion of clindamycin, a 100mg IV infusion of doxycycline (empirically due to the possibility of co-infection with other tick borne parasites) and also commenced on 650mg quinine PO TID. After the initial infusions, he was continued on 600mg clindamycin PO TID and on 100mg doxycycline PO BID. Repeat blood smear for parasites showed a rise in percentage parasitemia to 4.5% about five hours after commencing therapy. On the second day of admission, patient continued spiking fevers, also his was found to have 6% percentage parasitemia. The percentage parasitemia fell to 4% the third day of therapy. On the 4th day of treatment he developed symptoms of quinine toxicity (tinnitus and nightmares) medications were then changed to 250 mg daily doses of azithromycin (after a one time 500mg azithromycin dose) and 750mg atovaquone tablets Q12. The patient improved overall and was discharged after a 6 day hospital admission with a 1 percent parasitemia. He was followed as an out-patient; parasitemia resolved 4 days post-discharge. He completed a total of 3 days-clindamycin + quinine, 11 days atovaquone +

azithromycin and a 10 days course of doxycycline.

Case 3: In late July 2016, a 71 year old man with no significant past medical history presented to the ED with complaints of fever, chills, nausea and generalized body aches and jaundice of about one week duration. 2 day prior to presenting at the ED, he presented at an Urgent care centre due to these complaints. He was then started on antibiotics for a urinary tract infection after a urinalysis positive for nitrites and bacteria, his Hgb then was 13 g/dL, and platelet count was 36×109/L, creatinine of 1.4mg/dL and BUN of 34mg/dL. Patient did not get better so he presented to our hospital; at that time his vital signs revealed hypotension and physical examination was significant for icterus and confusion. Investigations showed that his Hgb had dropped to 9.6 g/dL, platelets were 40×109/L, BUN/ Creatinine ad risen to 99 mg/dL / 4.8 mg/dL. Haptoglobin was <8 mg/dL while liver enzymes, total bilirubin, LDH and D-dimer were all markedly elevated. Furthermore burr cells were present in his peripheral blood smear and he had reticulocytosis. Renal and abdominal ultrasounds were unremarkable. An assessment acute hemolytic anemia probably due to thrombotic thrombocytopenic purpura was made. He was admitted to the MICU required vasopressors support and also had a session of plasmaparesis.

On the second day of admission, 'parasites' were identified from blood specimen drawn at presentation. There was initially an uncertainty about whether the parasite was Babesia or Plasmodium. However, the working diagnosis of babesiosis was made because the patient had not travelled out of the country in the past 4-5 years (making malaria unlikely). He resided in Pennsylvania but travelled to Delaware about one month before the onset of symptoms. The patient engaged in gardening a lot but never noted a tick bite. He was HIV negative with no history of immunocompression and had a functioning spleen. Patient was stated on IV clindamycin 600mg Q 6 and oral quinine 324 Q 12 with doxycycline 100mg Q 12 (based on the possibility of co-infection with other tick borne illnesses like anaplasmosis, ehrlichiosis and Lyme disease).

On the second day of admission, he required exchange blood transfusion due to his downward trending Hgb (transfusion was initiated it fell to 8.0 g/dL) also analysis of blood drawn at presentation he had 12% parasitemia. In addition, on the second day of admission, hemodialysis (HD) was commenced due to declining renal function (dialysis was started creatinine reached a peak of 5.14 and GFR troughed at 11). The parasite load kept a constant downward trend- from 12% at presentation to 8.5% after plasmaparesis and further to 1 % Day 1 post-exchange blood transfusion. This percentage fell to < 1% day 3 post-exchange transfusion. The report of 'no blood parasite seen' was given day 6 post – exchange transfusion with the choice of antibiotics outlined earlier. Patient subsequently showed steady clinical improvement; was weaned off vasopressors, regained renal function (after a total of 3 HD sessions) and was transferred from the MICU to the general medical floors. He was eventually discharged to a skilled nursing facility; he spent a total of 12 days at the hospital. Discussion. Historically, severe babesiosis was thought to be a disease almost exclusive to immunocompromised and asplenic individuals; however there seems to be a shift away from this fact. As several cases of severe disease have

been reported to affect healthy immunocompetent, non-splenectomized adults.13,14 This is in concordance with the findings of this case series where all of the reported cases were all the affected individuals were previously healthy. Advanced age has been identified as a factor that increases the likelihood of developing symptomatic disease.15 The mean age of patients in this report was 68 years, all 3 patients suffered from symptomatic disease requiring hospitalization.

Even though Pennsylvania has historically not been considered as endemic for babesiosis recent literature suggests that the condition may be an emerging disease Eastern Pennsylvania, thus more local public awareness needs to be generated about this condition.16 Furthermore, the fact that the disease could be acquired from visiting other endemic nearby states should also make babesiosis a strong consideration in patients presenting in summer/spring (which typically is when babesia has it highest incidence) with classic features like fever/myalgia/jaundice in addition with laboratory findings indicative of hemolysis. Sadly, in two cases in this series the diagnosis was missed initially despite the fact that all patients had classic features, recent history of recent travel to other endemic states and suggestive laboratory findings.

As a consequence, investigation for babesiosis in the two cases was prompted only after parasites were incidentally found whilst blood samples were being manually processed for CBC. Ideally, babesiosis is should be diagnosed by microscopic examination of Geimsa- or Wright stained thin blood smears.17 Demonstration of parasites in a blood film provides definitive proof of current infection, multiple blood smears should be examined in the early stage of the illness as parasitemia is usually low then . 18 Polymerase chain reaction (PCR) is more sensitive than blood smears and also provides molecular characterization of the Babesia species. Serology with PCR testing of seropositive individuals is a good method of establishing the diagnosis in patients with low-level or transient parasitemia.19 It is recommended that symtomatic infection (proven by positive blood smears or PCR) lasting for longer than 3 months should be treated for 1 week with a combination of atovaquone and azithromycin.20

Treatment of mild to moderate disease treatment consists of a 7-10 days treatment with a combination of atovaquone and azithromycin.21 This regime is preferred to an equally effective combination of quinine and clindamycin because it has less adverse effects. Common side effects associated with the use of quinine and clindamycin are tinnitus, hearing loss and diarrhoea.22 In one case in this series , qunine / clindamycin therapy had to be discontinued after the patient developed tinnitus and disturbing nightmares while on therapy. Patients with one or more of the following risk factors typically develop severe disease: greater than 50 years, splenectomy, malignancy, immunosuppressive therapy, or HIV infection. It is worthy of note that cases in reported here developed severe disease with grave complications that included severe anemia, acute renal failure requiring hemodialysis, non-cardiac pulmonary edema, severe hypotension necessitating vasopressor support and ICU level of care. In these cases, clindamycin with quinine is preferred .20 In addition, partial or complete red cell exchange transfusion is indicated in patients with a

percentage parasitemia of 10% or greater; severe anemia ; renal/ hepatic or pulmonary impairment.23

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4.Radiographic Fusion of Multi-Level Anterior Cervical Decompression and Fusion with PEEK Interbody Implants and Local Autograft

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Introduction: Since its introduction in the 1950’s by Robinson and Smith, anterior cervical discectomy and fusion (ACDF) has become one of the most commonly performed spinal procedures.1 It is a highly successful surgical procedure for degenerative cervical disc disease associated with radiculopathy or myelopathy, its most common indication.2 The popularity of

ACDF stems from its accessibility and reliability of outcome.3,4 Nevertheless, the success rates decline in multi-level ACDF as the number of operated levels increase.2

One and two-level procedures utilizing ACDF are generally successful in the range of 95-100%, whereas most reports on multi-level ACDF demonstrate relatively high rates of pseudoarthrosis.5,6 It has been reported that non-fusion accounts for approximately 80% of spinal surgery failures.7 In addition, 20 to 30% of multi-level anterior cervical fusion procedures with autogenous bone may result in graft collapse.8 Autologous bone grafting has been associated with a number of complications including donor-site pain, infection, hematoma formation, iliac crest fracture and meralgia parasthetica.9 To prevent donor site morbidity, the use of polyetheretherketone (PEEK) interbody fusion cages in 1- and 2-level ACDF has demonstrated excellent outcomes, and deemed a viable alternative to tricortical autogenous bone grafts.10,11

Ideally, the PEEK interbody fusion cage should provide immediate stability, maintain spinal alignment, maintain foraminal height and achieve similar fusion rates with autografts.12 However, radiographic studies of PEEK interbody fusion cages in multi-level ACDF is scarce. The purpose of this retrospective study is to evaluate the radiographic evidence of fusion for multi-level ACDF using PEEK interbody fusion cages and local autograft. We hypothesize that multi-level ACDF with PEEK implants and local autograft will have improved rates of radiographic fusion than presented in the current literature.

Materials and Methods: The research and ethics committee at our institution determined that institutional review board approval was not required for this study. Ninety-five patients who underwent multilevel anterior cervical discectomy and fusion of three or more levels at our institution between 2008 and 2013 were included in our study. Of these, seventy patients had follow-up radiographs accessible for review. A total of two hundred and thirty-one levels were surgically treated in these seventy patients. Our study population consisted of thirty-eight females and thirty-two males who all underwent primary multilevel fusion for various indications including: cervical spondylosis, cervical radiculopathy, and/or cervical myelopathy. The age range was from thirty-three to seventy-one, with an average age of fifty-one. All patients with histories of prior cervical surgery or infection in the region were excluded. All surgeries were performed by a single board-certified orthopaedic spine surgeon along with an orthopaedic resident and physician assistant.

Operative Technique

A standard, anterior Smith-Robinson approach with a transverse incision was utilized for all cases. Anterior osteophytes were removed and discectomy was performed with pituitary rongeurs. Cartilaginous endplates were removed using curettes. The anterior inferior corners of the vertebral bodies were resected with a Kerrison for use as local autogenous bone graft for the level below. Afterwards, Kerrisons were used to resect the posterior bony margins and posterior longitudinal ligament. A cutting broach was used to prepare all interspaces. PEEK interbody devices were filled with local autogenous bone graft and then impacted into the interspaces. An anterior plate with screws was then applied. A Penrose drain was placed in the wound and the incision

was then closed in layers. An Aspen rigid cervical orthosis was applied and maintained for 1 week in the post-operative period.

Radiographic Analysis

X-ray studies of all patients were obtained at follow-up office visits. X-ray follow-up in our study ranged from four to eight months post-operative. Anterior-posterior and lateral x-rays were analyzed by a single board-certified musculoskeletal radiologist for radiographic evidence of fusion. Fusion was determined by the presence of bridging trabecular bone across the segment, no implant subsidence or migration, and maintained implant integrity and position. Each level was independently assessed for fusion and scored as having evidence of fusion, no evidence of fusion, or the radiologist was unable to determine whether fusion had occurred due to an inadequate study or obscuration.

Results: There were a total of seventy patients included in this study. Fifty one patients had a three-level anterior cervical decompression and fusion (73%), eighteen patients had a four-level surgery (26%) and one patient had a five-level surgery (1%). .

Sixty-two patients went on to fuse at all levels radiographically (88.5%). A total of eight patients did not demonstrate radiographic evidence of fusion at one or more levels (11.5%). One patient in this study did not show radiographic evidence of fusion at two of the four operated levels, and seven patients did not show radiographic evidence of fusion at one of the operated levels. There were no patients in this study that did not fuse at all operated levels.

Of the fifty-one patients that had a three-level ACDF, forty- seven demonstrated fusion at all operated levels (92%). Of the eighteen patients that had a four-level ACDF, fourteen patients demonstrated fusion at all levels (78%). One patient in this study had a five-level ACDF, and demonstrated fusion at all levels. Table 1. The total number of levels surgically treated with an ACDF among the seventy patients was two hundred and thirty-one. Two for C2-3, twenty-seven for C3-4, sixty-eight for C4-5, seventy for C5-6, sixty-one for C6-7 and three for C7-T1. At C2-3, two levels demonstrated radiographic evidence of fusion (100%). At C3-4, twenty-six levels demonstrated radiographic evidence of fusion (96%). At C4-5, sixty-six patients demonstrated radiographic evidence of fusion (97%). At C5-6, sixty-eight patients demonstrated radiographic evidence of fusion (97%). At C6-7, fifty-seven patients demonstrated radiographic evidence of fusion (93%). At C7-T1, three patients demonstrated radiographic evidence of fusion (100%). Table 2.

Number of Levels	Number of Patients	Radiographic Fusion	Not fused on radiograph
Three Levels	51	47	4
Four Levels	18	14	4
Five Levels	1	1	0

Table 1: Radiographic fusion based on number of surgical levels

Level	C2-3	C3-4	C4-5	C5-6	C6-7	C7-T1	Total
Number of Levels	2	27	68	70	61	3	231
Radiographic Fusion	2	26	66	68	57	3	222
Not fused on radiograph	0	1	2	2	4	0	9

Table 2: Radiographic fusion based on individual surgical levels

One patient in the study group did not fuse two of the four levels radiographically. Seven patients did not demonstrate radiographic evidence of fusion at one level. Of two hundred and thirty-one levels, two hundred and twenty-two demonstrated radiographic evidence of fusion (96%). A total of nine levels did not demonstrate signs of fusion (4%). Eight patients had radiographic evidence of mild anterior subluxation of the vertebral body compared with pre-operative radiographs. Of these eight patients, two patients had one level that did not demonstrate radiographic evidence of fusion. The remaining six patients demonstrated fusion at all levels. Three patients had evidence of osteolysis at a single level, of which one level did not demonstrate evidence of fusion. No other radiographic complications were noted.

Discussion: In our present study, we have demonstrated that multi-level ACDF with PEEK interbody implants and local autograft have significantly higher rates of radiographic fusion than previously reported. A total of two hundred and thirty-one levels were surgically treated among seventy patients. Of the seventy patients in the study, sixty-two patients fused at all levels. Of the two hundred and thirty one levels surgically treated, two hundred and twenty-two demonstrated radiographic evidence of fusion. Eighty-eight percent of patients went on to fuse at all levels (62/70), and of the two hundred and thirty one levels, ninety- six percent of the levels fused successfully (222/231).

It has been reported that a majority of spinal surgery failures stem from pseudoarthrosis, and that the rate of pseudoarthrosis increases with the number of levels treated in multi-level ACDF.5-7 One study demonstrated a non-union rate of fifty-four percent.14 Another study showed the nonunion rate for ACDF with plating was 2.9% in one-leve1, 5.4% in two-level, and 17.5% in three-level.15 Utilizing local autograft for the PEEK interbody implant, we were able to avoid the complications associated with bone graft harvesting. Autologous bone grafting has been associated with a number of complication. This includes donor-site pain, infection, hematoma formation, iliac crest fracture and meralgia paresthetica9. In our study, none of the patients had complications stemming from local bone graft harvesting.

Bone or hardware related complications have been reported after multi-level corpectomy and ACDF.13 In our present study, no cases of graft subsidence occurred. There were no hardware complications, and only three patients had evidence of osteolysis at a single level, of which one level did not show radiographic evidence of fusion.

Advantages of this study include that all of the surgeries were performed at a single institution

by a single fellowship trained spine surgeon. In addition, the x-rays were interpreted in a blinded manner by a single fellowship trained musculoskeletal radiologis.

Limitations of this present study include that it is retrospective. Second, the number of patients undergoing four and five level ACDF was small. In addition, we did not utilize flexion-extension radiographs or CT scans to assess the fusion.

Conclusion: In conclusion, multi-level ACDF is associated with a high level of radiographic fusion when using a PEEK interbody implant and local autograft. This technique is safe and effective, and may obviate the need for circumferential procedures.

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5.Bacteriological Etiology of Complicated Appendicitis in Children: one institution experience

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Introduction: Appendicitis is the most common cause of intra-abdominal infection and surgical intervention in children with a higher incidence in adolescents and young adults (1). Intra-abdominal abscesses were more frequently observed in perforated appendicitis than in non-perforated appendicitis. The pathogens from the normal enteric flora are involved in the pathology of intra-abdominal infections; often poly-microbial (74%) in nature and include both aerobic and anaerobic strains (2). The most frequently isolated bacteria are *Escherichia Coli* and *Bacteroides sp.* Other groups of bacteria isolated include Staphylococci, Streptococci, Pseudomonas, Klebsiella and other Enterobacteriace (2). Complicated intra-abdominal infections such as abscesses or peritonitis occur in about 23% of cases (3). Though *E. coli* remains the major strain identified, its frequency has decreased over time. Streptococci although less frequent in the normal intestinal microbiota, have been present at higher rates in the recent periods analyzed (3). It seems likely that the traditional practice of intraoperative peritoneal swabs during appendectomy has a role to play in increased identification of *Streptococcus* group. It is reasonable to recommend the culturing of peritoneal fluid if frank pus is found or in high risk patients (4, 5, 6). Though there is an ongoing discussion about the optimal antibiotic therapy after appendectomy for children, mono-therapy with broad spectrum agents is as effective and more cost effective then multi-drug therapy. Antibiotic selection should be reevaluated based on the local epidemiology and intra-operative cultures (7)

Objective: The goal of this study is to examine the bacteriological etiology of acute and complicated appendicitis in the pediatric population.

Methods: Scientific and ethics approval were obtained from the Institutional Review Board (IRB) prior to the study initiation. The study population is all pediatric patients (<18 years) with discharge diagnosis of appendicitis from May 2009 to March 2014 identified as study population. Retrospective Cohort was the chosen study method. All charts were reviewed and data was collected on history, clinical findings, radiographic imaging, length of stay, and choice of antibiotics. Information was gathered on operative findings and final histo-pathological report to define the type of appendicitis.

Microbiological culture and sensitivity report of peritoneal fluid and purulent material was used for the bacteriological data. All cultures were obtained using swab from the peritoneal fluid or purulent material. .

All patients with the diagnosis of appendicitis were divided into two groups. Patients with perforation, peritonitis, gangrenous and/or abscess were assigned to the complicated appendicitis (CA) group. Patients with mucosal, transmural and/or periappendicitis were

assigned to the uncomplicated appendicitis (UA) group. All available microbiological culture reports of peritoneal fluid were reviewed for the type of bacteria, mono or polymicrobial nature of culture isolates and sensitivity pattern. Statistical analysis was done using Chi-square test.

Results: Demography**:** A total of three hundred and eighty five patients were identified in the study period. Two hundred and eighty seven (74.5%) patients were classified as UA and ninety eight (25.4%) with CA. Peak occurrence of appendicitis. (40%) observed in the eleven to fifteen year age range; of which 24.8% were in the CA group. Only 11% of cases of appendicitis (45out of 385) were zero to five years of age range; however, 53% ($p<0.001$) of them (24 out of 45) had CA. So complications are significantly ($p<0.05$) increased in less than five years age group. Complications such as, perforation,

Results			
	Complicated	Uncomplicated	P value
Avg Age	11	10.5	0.9
SexRatio (Male/Female)	1.5	1.4	0.8
Avg Duration of hospital stay	6.6	1.9	<0.001
No of culture positive (%of total)	80	23	<0.001

Table 1.Summary of Data concerning the patients' demographics, type of appendicitis and their peritoneal samples

peritonitis or abscess noticeably increases the hospital stay of appendicitis patients. About 66% (65 out of 98) of patients with CA had hospital stay more than 5 days, yet 1%(3 out of 287) of UA hospital stay was more than five days. Average duration of hospital stay remained around 1.8 days in UA throughout the study period, nevertheless it was marginally decreased from seven to five and a half days in last four years in case of CA (Table 1). Difference increase in hospitalization days is statistically significant ($p<0.001$) in CA group. Bacterial culture report was available for 56% of UA and 96% of CA cases. Twenty two percent of UA cases were positive for bacteria, whereas 80% were positive in CA (Table 2). Almost 60% (56 out of 94) of CA cultures were polymicrobial, with *E. coli, Streptococcus* and *B. fragils* being the most commonly isolated pathogens, compared to 6% polymicrobial in UA. *E. coli* was isolated in 62% of CA followed by *Bacteroids* 60% and streptococcus group in 46%. Ten percent (10 of 94) of all CA cases were associated with post-operative intra-abdominal

abscess and 60% of these were caused by *Streptococci* group and rest had *Klebsiella pneumonie*, *B.fragilis, E. coli*. Presence of Streptococci in CA compared to UA was more statistically significant (p<0.001) than presence of Ecoli (p<0.018).

Type of Bacteria	CA culture positives (N=75)	UA culture Positives (N=27)	P value
Escherichia coli	47 (62%)	9 (33%)	<0.018
Streptococcus sp	35 (46%)	4 (15%)	<0.001
Bacteroides fragilis	45 (60%)	7 (26%)	<0.017

Table 2: Bacteriology of Complicated vs Uncomplicated culture positive Appendicitis

No of cases	*E. coli + Streptococcus + B. fragilis*	*E. coli + Streptococcus*	*E. coli + B. fragilis*	*Streptococcus + B. fragilis*
Complicated	9	12	14	9
Uncomplicated	0	0	5	1

Table 3: Cases of mixed infection of E. coli, Streptococcus and B. fragilis

Discussion: Peritoneal fluids from 80% (75 0f 94) of cases of complicated appendicitis were culture positive with 43% total positive culture rate. This is consistent with previous studies showing culture positive rate varying from 24 to 57% (8, 9). The bacteriology of complicated appendicitis has been described in several studies and invariably includes a mixture of aerobic and anaerobic enteric flora (5, 7, 8, 9). In our series, the most frequently isolated organisms were *E. coli, Streptococcus of alpha hemolytic non group D, Streptococcus milleri* group, and *Bacteroides fragilis*. Other bacteria like *Peptostreptococcus, Fusobacterium, Pseudomonas aeroginosa, Kleibsella pneumonie, Enterococcus fecalis* were also found in few cases. Most of the complicated cases in this series consist of a collection of pathogens in various combinations. Among all identified bacteria, *Streptococcus* is not a dominant pathogen in normal intestinal micro biota, especially in children (4). This study found 46% cases of CA were culture positive for different types of *Streptococcus* either alone or in group, in which alpha hemolytic non group D (47% of streptococcal positive) and group Milleri (30% of streptococcal positive) are leading strains. Eighty percent of these

streptococcal culture positive cases were associated with appediceal abscess formation. Alpha hemolytic *non group D Streptococcus* has been seen as a neonatal sepsis pathogen (12) and not been reported as a widespread causative agent in appendicitis. Presence of *Streptococcal milleri* has been associated with a 7-fold increase in abscess formation (13); prolonged hospital stay and longer use of antibiotics in patients with an abscess after appendectomy (2, 7). Ten percent of our complicated appendicitis(10 of 94) patients had post-operative intra-abdominal abscess and 40% of them were positive for *S. milleri. S. milleri* plays an important role in infections of internal organs and certain body fluids such as central nervous system (e.g. brain abscess, meningitis), pyogenic liver abscess and appendicitis. S. *milleri* as the source of bacteremia may perhaps be an indication of a hidden abscess. .

The propensity of *S. milleri* for pyogenic infections remains unclear; however, it is hypothesized that prophylactic use of antibiotics such as Gentamicin and Metronidazole may enhance *S. milleri* overgrowth (2, 14, 15). The combination of pathogens and their frequency in polymicrobial samples shown in Table 3 clearly demonstrates more polymicrobial culture positive in CA group. It is interesting to note that higher numbers of strains were identified in each polymicrobial sample from more recent years. Studies shows that another factor that may have played a role in higher yield of peritoneal samples is, prompt transport of the peritoneal fluid samples from the operating room in an occluded syringe and its immediate plating on the culture medium particularly for anaerobic strains (7, 9). .

However, this increase cannot be accounted for by a change in bacterial identification techniques since our institutional method of collection of specimen from the operating room, transport of the sample and plating of the swabs in the microbiology lab has not changed in the past ten years.

A previous study identified *E. coli* as a major mono-microbial pathogen in up to 88 % of culture positive CA (10). Though *E. coli* is a common pathogen identified throughout our study period, its presence as a single pathogen represented only 5% of CA in comparison to 17% of UA. But overall presence of E.coli in CA compared to UA is statistically significant ($p<0.018$). Yet overall presence of Streptococci in CA is more statistically significant ($p<0.001$). *E. coli* with *Streptococcal* species was found in 24.6% of CA which is strong evidence that *Streptococci* can be implicated in causing complications.

The presence of *Bacteroides fragilis* varies from 18.9 to 44.9 % in CA in previous studies (3, 11). This study finds 47.9% of our CA samples positive for *B. fragilis* either alone or in combination. Other anaerobes such as *Peptostreptococcus* have been shown to be decreased from 16.7% to 0% over 20 years in previous studies (3). Our data finds *Peptostreptococcus* present in 15% of CA. All anaerobes isolated were reported to be sensitive to Piperacillin-tazobactum and Metronidazole.

According to previous studies, the incidence of *Pseudomonas aeruginosa* in cases of perforated appendicitis is highly variable from 19% to 58% of peritoneal samples cultures (6, 7). In this series *P. aeroginosa* was isolated in 6% of culture positive CA. In our study the most commonly used empirical antibiotic is

Piperacillin-tazobactam and the organisms isolated were susceptible to it. The second highest used antibiotic is third generation cephalosporin with metronidazole or clindamycin which is also recommended by some studies (16, 17).

Conclusion: Children with CA showed increased incidence ($p<0.001$) of alpha hemolytic non group D streptococcus and streptococcus milleri infections then E coli. Majority (80%) of strep positive events are associated with abscess formation.

Limitation: Culture reports were available for only 56% of the uncomplicated appendicitis patients. It is a single center reporting.

Future Directive: Research on changing epidemiology of bacterial etiology of appendicitis and selective use of antibiotics as directed by culture reports.

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6.Right Ventricular STEMI disguised as Myxedema Coma: A Case Highlighting Diagnostic Difficulty

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Background: Isolated right ventricular (RV) infarcts are significantly less common than left ventricular infarcts. However, nearly 50% of all inferior myocardial infarcts involve the right ventricle (1). In a meta-analysis study, the mortality rate in the presence of right ventricular infarction was noted to be higher (17%) than in its absence (6.3%). The worse outcome is attributable to the high incidence of refractory cardiogenic shock as evidenced in

this particular patient. Infarcted RV tissue is unable to provide sufficient preload which is in turn, essential for adequate left ventricular performance (3.). .

Case : A 74 year old female presented to the emergency department at the urging of her family for hot flashes, lethargy, and fatigue for 3 days. She had not been seen by a physician in decades. She denied any symptoms of cardiac discomfort. On physical exam, she was found to be bradycardic with a heart rate in the 40's, hypothermic to 95.5F rectally and hypotensive to 60/40 mmHg. Cardiac exam revealed normal heart sounds with no jugular venous distension, lungs were clear to auscultation. +1-2 pitting edema bilaterally. Pertinent laboratory findings included WBC 10.9 with 9 bands, Hb: 16.5, creatinine, 1.18, ALP: 36, ALT: 2.8, AST: 107, lactate 8.3, troponin 0.954 µg/L, and TSH: 32.7. EKG (Figure 1) was initially read as sinus bradycardia at 43 with low voltage. CT head and chest x-ray were unremarkable. She was admitted to the intensive care unit and treated as myxedema coma versus septic shock. The patient was given intravenous levothyroxine, stress dose steroids, fluids, broad spectrum antibiotics, and intubated due to declining mental status. She was aspirin loaded and started on a heparin drip for elevated troponin. Subsequent troponins resulted as 35 µg/L and then >74 µg/L. The patient received an echocardiogram that revealed a severely dilated RV with severe systolic dysfunction. The left ventricle was normal.

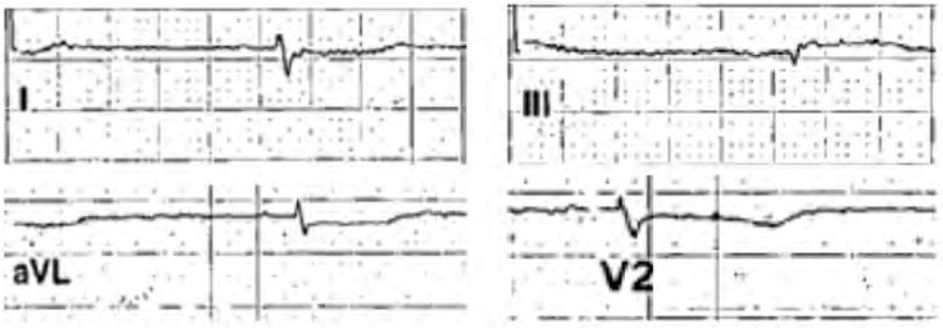

Fig 1: Selected EKG leads demonstrating ST segment changes in setting of low voltage.

Due to the echocardiogram, a closer look at the EKG revealed subtle 1mm ST elevations in the inferior distribution with ST depressions in the anterior and lateral leads. Low voltage of the admission EKG resulted in the masking of these critical findings. She was diagnosed with an isolated right ventricular infarct, received several liters of fluid resuscitation, and a dobutamine drip was initiated for cardiogenic shock. The patient initially refused, but ultimately underwent a left and right heart catheterization that revealed elevated right sided filling pressures with low cardiac output, normal wedge pressure, and multi-vessel coronary artery disease (CAD). A 99% right coronary artery lesion was stented. An intra-aortic balloon pump was also inserted to augment cardiac output. Despite these measures, the patient remained in refractory shock. Patient and family did not desire aggressive management, resulting in eventual death.

Discussion: This patient's case particularly highlights the diagnostic difficulty of identifying a right ventricular ST-elevation myocardial infarction (STEMI) in the setting of a patient with no previous medical care and multiple confounding factors. Severe hypothyroidism is associated with altered mental status, bradycardia, hypothermia and hypotension without overt cardiac symptoms. In some instances, myxedema coma can be associated with the development of a pericardial effusion that can result in low voltage on an EKG. Additionally complicating her clinical picture, the patient experienced symptoms of lethargy and fatigue for several days prior to presentation, but her troponin trend was more characteristic of an acute coronary syndrome (ACS) that occurred on the day of admission. In fact, her initial elevation in troponin could have been attributable to demand ischemia secondary to sepsis as she presented with a bandemia, elevated lactate and hypotension. While the etiology of her symptoms is clearly right ventricular failure in hindsight, it is important to note that at the time of initial presentation, the physical exam findings were more indicative of myxedema coma than isolated right ventricular infarction. In this particular case, the importance of diagnosing an RV STEMI was especially key, as the usual treatment for myxedema coma involves intravenous thyroxine. Exogenous thyroid hormone is harmful in the setting of ACS as it increases cardiac demand, and can lead to further myocardial ischemia.

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Case Reports

1.Dysphagia, Hoarseness, and Facial Paresthesia: a Triad of Cervical Diffuse Idiopathic Skeletal Hyperosteosis Syndrome

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Introduction: Diffuse Idiopathic Skeletal Hyperostosis (DISH) is characterized by unique, flowing calcifications of the contiguous vertebrae of the spine, spinal ligaments, and entheses. It presents as the neck, thoracic spine, low back, and/or extremity pain and spinal morning stiffness.(1,2).
Case: We report a case of progressive dysphagia, hoarseness and trigeminal spinal nucleus involvement secondary to severe DISH. An 85-year-old-female with h/o hypertension presented with 2-3 months of a progressive cough, difficulty clearing mucus, dysphagia to solids, hoarseness and left sided paresthesia primarily localized to the left sided shoulder, hemiface, neck, upper extremity and torso. Examination revealed diminished vibration and temperature sense along with paresthesia of left side of the face. Initial stroke workup including head CT, Brain MRI, MRA of head/neck and echocardiogram were unremarkable. Swallow evaluation disclosed pharyngeal-esophageal dysphagia. A CT-scan soft-tissue neck and MRI-Cervical Spine revealed diffuse anterior syndesmophytes in C1-T1 vertebrae with ossification of the anterior longitudinal ligament and an osteophyte compressing the cervical esophagus and posterior trachea. Ligamentum flavum was hypertrophied resulting in mild to moderate central spinal stenosis, cord compression and bilateral moderate C1-C5 neuro-foraminal stenosis explaining neurological symptoms. This was consistent with DISH syndrome.
Discussion: DISH is diagnosed by Resnick's Criteria. Always check CBC, ESR, liver enzymes, calcium, phosphate, PTH, IGFs/Growth Hormone levels and SPEP to exclude possible etiologies of hyperostosis. DISH as possible etiology of unexplained dysphagia, hoarseness and paresthesias is rare and should be sought out in elderly, as surgical resection of local cervical spurs can be palliative to resolve symptoms.

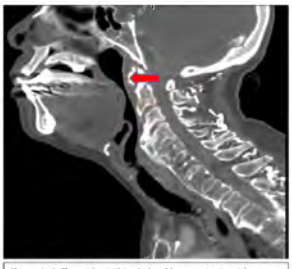

Figure 1: Diffuse idiopathic skeletal hyperostosis with compression of the esophagus and larynx

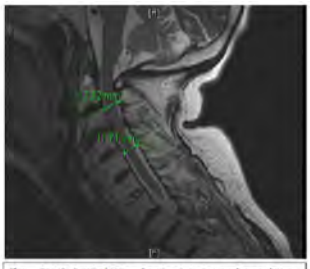

Figure 2: MRI Cervical Spine showing Anterior syndesmophytes C4-T1 > Spine stenosis + cord compression + syndesmophytes encroaching cervical esophagus.

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2.A Case of Falsely Low Serum Bicarbonate Secondary to Hypertriglyceridemia

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Introduction: Serum bicarbonate (HCO3) levels are often looked at during initial laboratory testing and can be the first indication of acid-base disturbances. There have been a limited number of case reports regarding irregularities in HCO3 collected on a basic metabolic panel (BMP) indicating an acidosis due to assay interference, such as hypertriglyceridemia or paraproteinemia. Here we describe a case where high triglyceride levels caused significant interference with our chemistry assay to give a falsely low serum HCO3 value.
Case: Our patient was a 60 year-old-male with type-2-diabetes mellitus, hyperlipidemia, hypertension, and congestive heart failure who presented with a one day history of shortness of breath and fatigue, non-exertional substernal chest tightness, palpitations and nausea. Home medications included fenofibrate and simvastatin. Initial labs were remarkable for: sodium 127 mEq/L, BMP HCO3 <5 mEq/L with an anion gap of 20, glucose 327 mg/dL, pH 7.397 and ABG HCO3 of 22 mEq/L. It was presumed that the patient had a mixed anion-gap and non-gap metabolic acidosis, with a concomitant respiratory acidosis. BMP was checked three additional times on alternative machines and ABG was repeated on a separate machine, with unchanged values. A triglyceride (TG) level was obtained after ultra centrifugation of the lipid sample, which was 3751 mg/dL. A BMP was thereafter obtained after ultra-centrifugation, with a HCO3 of 18 mEq/L.
Conclusion: This case represents a significantly elevated TG level causing assay interference, resulting in a "pseudohypobicarbonatemia". It was determined that these chemistry machines had only been verified up to a TG level of 2000 mg/dL.

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3.Drug induced Lupus: a rare cause of splenomegaly

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INTRODUCTION: Hydralazine rarely causes DIL (Drug induced lupus). It can present with atypical symptoms including type B symptoms, Serositis and Hepatosplenomegaly. High clinical suspicion is required for diagnosis. Labs include positive Anti-histone antibodies, rare anti double stranded DNA antibodies, anemia and Leukopenia. Other etiologies including SLE, malignancy (for example lymphoma), and chronic infections (for example HIV, Hepatitis

B/C) need to be excluded.

CASE: We report a case of 65 year old man with history of hypertension, hyperlipidemia, Splenomegaly presenting to Emergency department with c/o Dyspnea for 3 days. On Lung exam he had decreased breath sounds on left lung base with dullness to percussion. His labs showed Neutropenia and anemia. His chest x ray showed large left sided pleural effusion. Thoracentesis was performed however his pleural effusion re accumulated in 2 days. Patient had positive anti histone Ig G antibodies with titer of 9.9 and ANA titers of 1:1280. Anti-smith/ double stranded DNA antibodies, RF, Anti Ro/La, anti RNP antibodies were negative. He was diagnosed with Hydralazine induced Lupus. No pathology was found after Splenectomy and repeat Bone marrow biopsy. He reported resolution of symptoms with discontinuation of Hydralazine and steroid therapy at 6 week follow up. There was complete resolution of his Pleural effusion. His antibody titers trended down on repeat lab work done at 6 months. Other causes including SLE (Systemic lupus), malignancy, and chronic infections were ruled out.

CONCLUSION: Early diagnosis and followup of DIL can prevent unnecessary invasive procedures in patients such as splenectomy in our patient.

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5. McKinnon RA, Nebert DW. Possible role of cytochromes P450 in lupus erythematosus and related disorders. Lupus 1994; 3:473.
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4.Role Of Endomyocardial Biopsy In The Diagnosis Of Cardiac Amyloidosis

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**Abington Memorial Hospital: Department of Medicine, Division of Internal Medicine
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Background: Wild-type senile Amyloidosis due to transthyretin deposition (ATTR) predominantly accumulates in the heart and is diagnosed rarely after age 60, manifesting as a restrictive cardiomyopathy1.

Case: An 80 y/o -male with ulcerative colitis had recurrent pleural effusions, requiring thoracentesis yielding borderline exudative fluid negative for infection and malignant cells. Three weeks ago he was diagnosed with Rheumatoid arthritis. He was readmitted with gradually worsening pedal edema, weight gain and worsening exertional dyspnea. Labs showed elevated alkaline phosphate (ALP), elevated cardiac BNP and new subnephrotic range proteinuria. Chest- X--r ay=pulmonary edema and large left recurrent pleural effusion. Echocardiogram normal left ventricular EF, grade 2 diastolic dysfunction with impaired relaxation and speckled myocardial pattern. Decision-making: Given the history of ulcerative colitis, rheumatoid arthritis, elevated ALP and new proteinuria along with the constellation signs of restrictive heart failure, a diagnosis of infiltrative cardiomyopathy was considered. SPEP=polyclonal IgG elevation. 24 hours urine

protein electrophoresis=normal. Abdominal fat pad biopsy=negative for amyloidosis. Given the high clinical suspicion for amyloidosis, an endomyocardial biopsy (EMB) was done showing amyloid deposition. The mass spectrometry was positive for wild-type amyloidosis. Prednisone and doxycycline were started.

Conclusion: Our case highlights three teaching points. 1) EMB should be pursued if an initial biopsy of peripheral tissues is negative and clinical suspicion is still high for cardiac amyloidosis. 2) An EMB provides specific information and defining the type of amyloid deposits is crucial for treatment2. 3) Doxycycline was selected as it is shown to disrupts transthyretin (ATTR) amyloid fibrils in transgenic mouse models.

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5.Scrotal Ulcer in a 43 year old male: A Diagnostic Challenge

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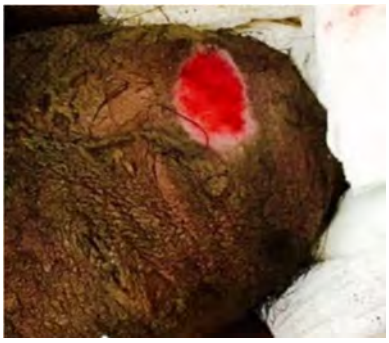
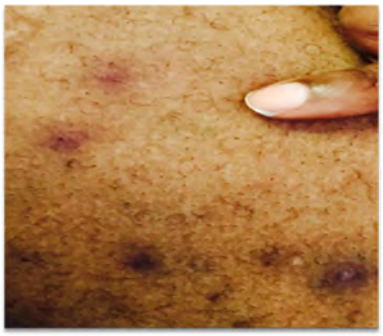
***Drexel University College of Medicine: Department of Medicine, Division of Rheumatolog

Case Description: A 43-year-old AAM with PMH of pulmonary hypertension and DVT presented with scrotal pain and ulcer. He also complained of leg swelli3ng, fever, chills, night sweats, and weight loss. He had a similar episode in the past which resolved after debridement, corticosteroids, and antibiotics. Examination revealed 2.5cm ulcer with granulation tissue on the scrotum, tender inguinal lymphadenopathy, bilateral lower extremity edema, left calf tenderness, and multiple hyper-pigmented macules and papules on the trunk and extremities. Lab work revealed elevated WBC, ESR and CRP; and positive tuberculosis screening test, blood (MRSE), and wound culture (K. pneumoniae). CTAP showed epididymal orchitis, skin defect and cellulitis in the scrotum; and LE duplex revealed stable chronic bilateral popliteal vein thrombosis. Histopathology of the ulcer and skin lesions was non-specific.





Discussion: BD is a rare, multi-systemic, auto-inflammatory disease that is more common in the Mediterranean and the Middle East1,2. The International Criteria for BD outlines classification criteria with ≥ 4 points needed for diagnosis3. Our patient's ICBD point score was six: scrotal ulcer (2-points), oral ulcer (2-points), acneiform-skin eruption (1-point), and venous thrombosis (1-point). Treatment includes steroids and/or immunosuppressive therapy and is geared towards clinical manifestations1,2,3. Steroids were held due to underlying infection. He was treated with warfarin for DVT, antibiotics for infection, and colchicine for oral ulcer. Early diagnosis and referral to a specialty center is recommended for comprehensive treatment3. No consensus exists regarding the course of the condition. Follow up on a regular basis to evaluate further systemic involvement is recommended.

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6.A Novel Approach to Anticoagulation in Thromboangiits Obliterans

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**Drexel University College of Medicine: Department of Family, Community and Preventive

Introduction: Thromboangiitis obliterans is a small and medium sized vessel vasculitis that causes progressive limb pain and thrombotic occlusion. It primarily affects males with a history of heavy, long term tobacco use. Although tobacco cessation is the mainstay of treatment, no additional strategies currently exist to treat and prevent recurrent thrombotic disease. We present a case utilizing multiple anticoagulation modalities to manage this issue. **Case**: A 45-year-old female with previous arterial thrombus on Coumadin presented complaining of bilateral lower and left upper extremity pain and claudication and was found to have multiple arterial occlusions despite a negative hypercoagulable workup. The patient's occlusions were persistent despite IR-guided tPA and subsequent tPA/heparin drip. Due to her recurrent thrombi, the patient was discharged on Aspirin, Clopidogrel, Enoxaparin, and Cilostazol with PCP and Vascular Surgery follow-up. The patient had regular outpatient follow-up and was able to temporarily cut down on cigarette smoking, but within 6 months, had developed further arterial occlusions. **Discussion**: Presently there is no definitive treatment for the disease or thrombotic occlusion prophylaxis. Isolated case reports have shown temporary relief with Cilostazol, though a Cochrane Review did not find an RCT that assessed Cilostazol, Clopidogrel, or Pentoxifylline. It did note that prostacyclin analogues could be more effective than Aspirin for rest pain, but not more effective than placebo. More research is needed to assess different methods of thrombotic prophylaxis.

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7.Ascending Paresthesia in a Middle-aged Male

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Case: A 38 year old caucasian male presented to the emergency room with ascending paresthesia of bilateral arms, legs and chest wall for 5 days without any motor weakness. There was no history of trauma, infections or vaccination. He had decreased sensation to pinprick, touch and temperature in all four extremities and chest with a sensory level of fourth cervical spinal cord level. Motor and cranial nerve examinations were normal. Laboratory studies were unremarkable. Spinal fluid analysis showed mildly elevated white cell count (10/mm3) with lymphocyte predominance. CSF Protein was normal. Neuromyelitis Optica (NMO) Antibody and Myelin basic protein assay were negative. MRI of Cervical spine with and without Gadolinium (Fig1) showed T2 hyperintense enhancing lesion at C4-C5 level suggestive of Longitudinally Extensive Transverse Myelitis (LETM). Patient was empirically treated with one gram methylprednisolone daily followed by tapering doses of steroids for 2 weeks. He had gradual resolution of his symptoms in three weeks.

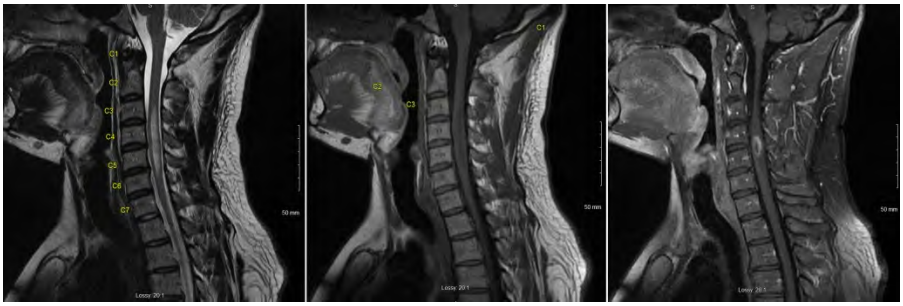

Fig 1. Sagittal section MRI of the cervical spine using gadolinium. Left T1 weighted post gadolinium contrast

Discussion: LETM is a spinal cord lesion involving three or more vertebrae on MRI of spine due to immune-mediated demyelination. Clinically, it presents as acute paraparesis or quadriparesis, sensory impairment, sphincter or autonomic dysfunction which evolve in hours to days. LETM is a typical finding of NMO, but can be associated with Multiple Sclerosis1, sarcoidosis, SLE2, and post-infectious myelitis.3,4 Bilateral symptoms with a spinal cord level on clinical examination, MRI findings and CSF pleocytosis help in diagnosis. It is treated with high dose glucocorticoids. For patients unresponsive to glucocorticoids, plasma exchange can be considered.

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8.Invasive Lipoma in a Family Medicine Outpatient Office

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Case: 49-year-old female presenting with two-weeks of worsening right upper arm swelling associated with a dull, heavy, throbbing feeling worsening with arm movement. She denied trauma, fever, skin redness or warmth, skin breakdown, discharge, or overuse. Physical exam uncovered a 4 x 5cm tender, rubbery, partially motile mass at the distal bicep that did not change with bicep flexion. Ultra sound, figure 1, demonstrated a hypoechoic mass with some abnormal features recommending MRI, figure 2, to exclude an aggressive neoplasm. The mass was surgically excised in entirety without complication showing a 6.5 x 6 x 2.4cm infiltrating lipoma without evidence of malignancy.

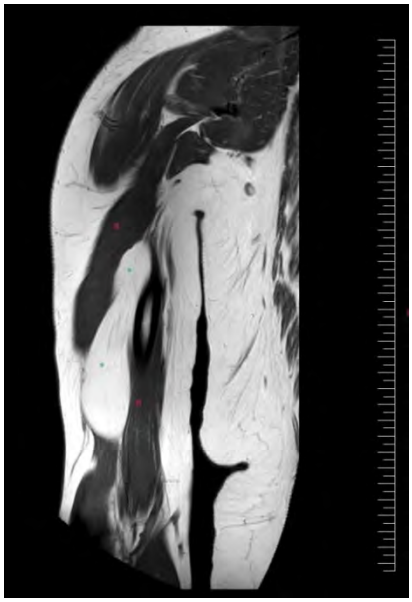

Fig 1 (right)- Well circumscribed mass between two biceps head

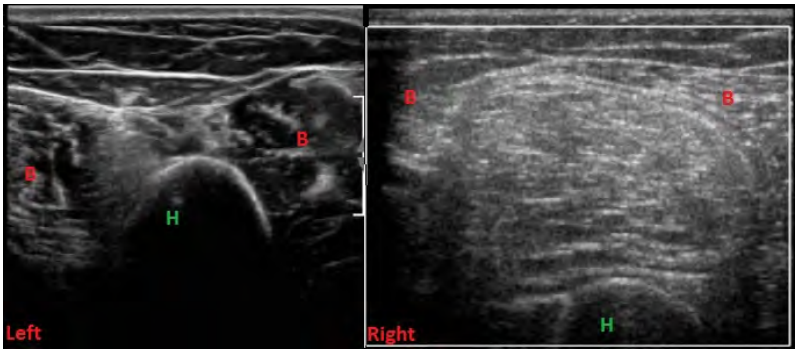

Fig 2: left, normal ultrasound biceps directly anterior to humerus Right: Solid invasive maas anterior to humerus but deep to biceps

Discussion: Lipomas are slow growing, fibrously encapsulated, adipose filled soft tissue tumors occurring in 1-2% of the general population[1]. These tumors are soft to the touch, motile, often painless, usually about 1–3 cm in size, most commonly found in adults 40 to 60 years of age and are typically superficial but can rarely infiltrate deep inter-muscular and/or intra-muscularly[2]. While most lipomas are benign evaluation for potential malignancy is important to avoid misdiagnosis since up to 1% of these lesions can show sarcomatous differentiation[3]. Prognosis of liposarcomas varies from 5 year survival of 56%-100% depending on site of origin, tumor size and depth, histological subtype and proximity to lymph nodes[4]. Treatment of lipomas is rarely necessary, but can be performed for cosmetic reasons, pain, movement restriction, or malignant workup. Surgical removal has a recurrence rate of 1–2% because complete surgical removal of deep lipomas is not always possible[5].

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2. Zamora, M. and e. al, High-Resolution Ultrasonography in an Aggressive Thenar Intramuscular Lipoma. JUM 2005. 24(8): p. 1151-1155.
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4. Song, C., et al., Management and Prevention of Recurrent Paratesticular Liposarcoma. Malays J Med Sci, 2013. 20(4): p. 95–97.
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9.Back Pain: A Crystal Clear Cause

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**Drexel University College of Medicine: Pathology-Anatomic and Clinical
***Drexel University College of Medicine: Department of Medicine, Division of Internal Medicine

Introduction: A 72 year old woman with a history of non-Hodgkins lymphoma, treated 15 years prior, presented with worsening, constant, throbbing left hip and lower back pain associated with numbness and tingling for three months, with acute worsening for the past three days. Physical exam showed left hip tenderness with decreased sensation and range of motion of the left leg.MRI of the lumbar spine showed a nonenhancing epidural lesion between L3-L5 and compression of the cauda equina with a differential diagnosis of extruding disc vs lymphomatous infiltration given her history of lymphoma. The patient was treated with decadron and neurosurgical decompensation with L3-L4 laminectomy with resolution of symptoms. Pathology revealed polarizable crystalline material suggestive of pseudogout.

Discussion: Pseudogout in the lumbar spine is rare (2,3). Commonly affected areas are the knee, wrist, elbow, and ankle. If spinal deposition of crystals occurs, it more likely affects cervical vertebrae rather than lumbar (4). Deposition in this patient occurred in the spine causing possible disc herniation which could be explained by the immediate relief after receiving decadron even prior to the surgical intervention. It is unclear why she developed CPPD disease in the spine with no predisposing factors. Despite the prevalence of back pain (1),

the differential remains wide and CPPD should be considered.

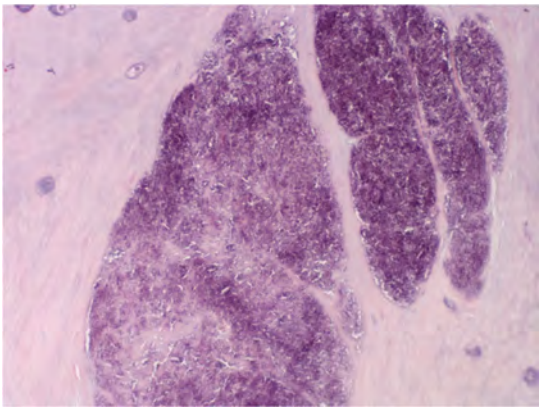

Image 1 Portion of intervertebral disc with basophilic crystalline deposition (H&E stain, 10xmagnification

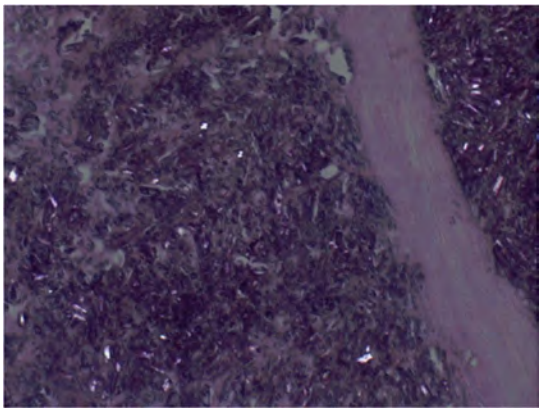

Image 2 : Small polarizable rectangular or rhomboid crystal within the disc (H&E stain, polarized, 40x)

Ref. 1.Shmagel A, Foley R, Ibrahim H. Epidemiology of Chronic Low Back Pain in US Adults: Data From the 2009-2010 National Health and Nutrition Examination Survey. Arthritis Care Res (Hoboken). 2016 Nov;68(11):1688-1694. doi: 10.1002/acr.22890.;
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10.Acquired Dual Coronary Artery Fistulas to Pulmonary Artery Found Many Years After Open Heart Surgery

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Introduction: Coronary artery fistula is an abnormal connection between one of the coronary arteries and a heart chamber or another blood vessel. We present a case of dual coronary artery fistulas to pulmonary artery which were found incidentally on cardiac catheterization many years after open heart surgery.

Case: Our patient is a 41-year-old female who presents with acute onset of dyspnea for one day. Her medical history includes bioprosthetic mitral valve replacement 13 years ago due to severe mitral valve regurgitation, atrial fibrillation, and diastolic heart failure. She was found to be in atrial fibrillation and heart failure due to medication non-compliance. Examination revealed an elevated jugular venous pressure, 3/6 holo systolic murmur in the apex radiating towards the axilla and pedal edema. Echocardiography revealed severe mitral valve regurgitation. The patient was evaluated for mitral valve replacement with right and left heart catheterization which incidentally revealed two coronary artery fistulas from the proximal left anterior descending [Figure 1] and right coronary artery

[Figure 2] to pulmonary arteries which were never present previously in her life. She was then transferred to a tertiary care center for surgical intervention.

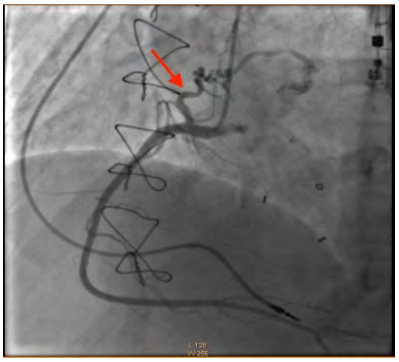

Fig 1

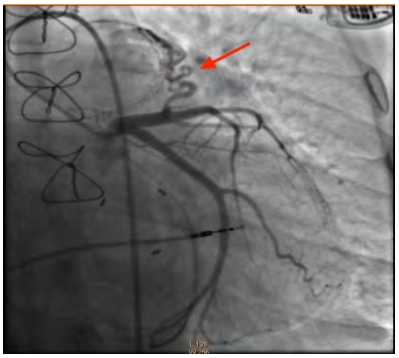

Fig 2

Discussion: Coronary artery fistula can be congenital or acquired [1] Acquired coronary artery fistula has been reported after open heart surgery. [2] Imaging modalities such as echocardiography, coronary angiography, multidetector CT angiography can be used for diagnosis. Treatment of choice is surgical intervention. [3] Complications include thrombosis, heart failure, atrial fibrillation, rupture, endocarditis, endarteritis, "steal" phenomenon from adjacent myocardium and arrhythmias. [4]

Ref. 1. Luo L, Kebede S, Wu S, Stouffer GA. Coronary artery fistulae. Am J Med Sci. 2006 Aug;332(2):79-84.
2. Jebara VA, Sarkis A, Acar C. Coronary artery-left ventricle fistula after cardiac surgery. Am Heart J 1981;122:1759–62
3. Said SA, Nijhuis RL, Op den Akker JW, et al. Diagnostic and therapeutic approach of congenital solitary coronary artery fistulas in adults: Dutch case series and review of literature. Neth Heart J. 2011 Apr;19(4):183-91.
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11.Pregnancy Related Spontaneous Left and Right Coronary Artery Dissection

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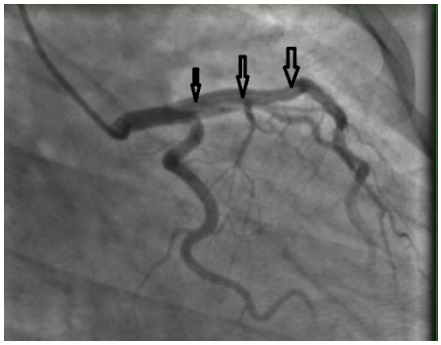
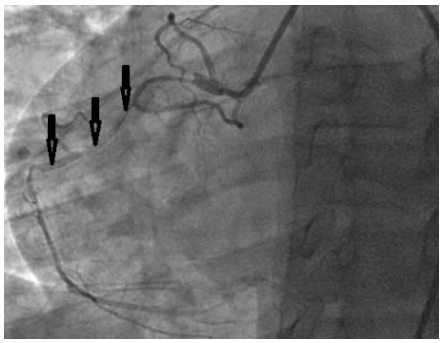
**Abington Memorial Hospital: Department of Medicine, Division of Internal Medicine
***Abington Memorial Hospital: Department of Medicine, Division of Cardiology

Introduction: Spontaneous coronary artery dissection (SCAD) is an uncommon cause of acute coronary syndrome, occurring predominantly in women during or immediately after pregnancy(1). The exact etiology is unknown. Below is a very interesting case of a middle age Afro-American women who had coronary arterial dissection of both right and left coronary artery within 7 days post-partum.
Case: A 35 years old female with no past medical history and recently delivered healthy baby via C-section presented to ER with chief complaint of chest pain and left shoulder numbness. Initial EKG showed ST segment elevation in leads aVL, V2 and V3. Emergent cardiac catheterization was performed which showed left coronary artery dissection (LAD) extending from the ostium till the mid vessel. It was managed medically. 2 days later patient developed new onset of chest pain, diaphoresis

and hypotension. EKG revealed ST segment elevation in leads II, III and aVF. Urgent coronary angiography was performed which this time revealed right coronary artery dissection not amendable to percutaneous intervention. Patient was in cardiogenic shock and was taken to cardio thoracic surgery with successful coronary artery bypass graft to LAD and RCA. Patient recovered well and was discharged to home on day 8th.



Left catheterization



right catheterization

Discussion: It is uncertain whether pregnancy independently increases risk for SCAD, but this possibility is certainly concerning. A high index of suspicion is critically important when dealing with any young woman presenting with chest pain associated with pregnancy. A timely diagnosis of this fatal condition helps early intervention and a successful outcome(2).

Ref. 1)Bac DJ, Lotgering FK, Verkaaik AP, Deckers JW. Spontaneous coronary artery dissection during pregnancy and postpartum. Eur Heart J. 1995;16:136–8
2)Kearney P, Singh H, Hutter J, Khan S, Lee G, Lucey J. Spontaneous coronary artery dissection: A report of three cases and review of the literature. Postgrad Med J. 1993;69:940–5

12.Cardiovascular Imaging For Single Coronary Arterial Trunk Arising From The Right Aortic Sinus

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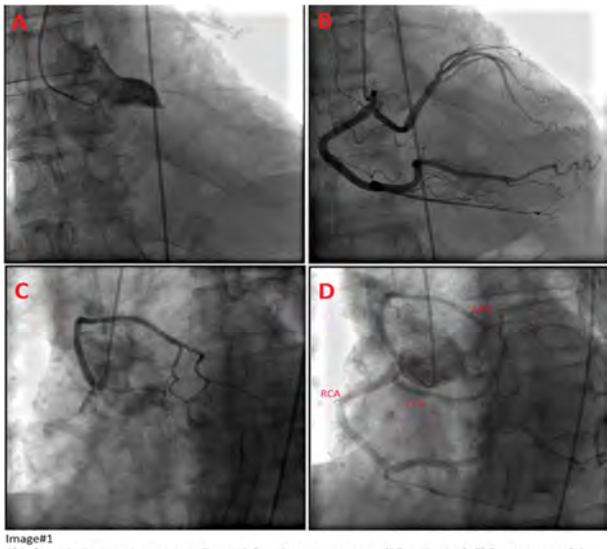
**Drexel University College of Medicine: Cardiovascular Disease
***Drexel University College of Medicine: Department of Radiologic Sciences
****Drexel University College of Medicine: Department of Medicine, Division of Cardiology

Introduction: Origination of the left coronary artery from the right aortic sinus occurs in 0.15% of CAA. The course of the anomalous artery becomes important clinically. If it crosses between the great vessels it may lead to extrinsic compression whereas a pre-pulmonic course is less malignant.

Case: 58 year old male was seen in cardiac consultation after post-operative C3-4 pre-vertebal cervical abscess washout for substernal chest pressure that radiated to both arms. EKG showed no abnormalities and initial serum troponin was <0.03. The troponin peaked at 4.7. Echocardiogram showed new septal wall hypokinesis with a grossly normal LVEF. Given the patient's new NSTEMI, left heart

catheterization was performed. It showed a single large trunk that arose from the right aortic sinus and gave way to the three main coronary arteries. The LCX arose from the proximal RCA. The LAD didn't reach the apex. Lastly, the PDA which had an RCA origin, wrapped around the apex and supplied the anterior lateral wall. Cardiac CTA confirmed a single coronary artery branching into the RCA, LCX, and LAD, which followed a pre-pulmonic course. There was no extrinsic compression by the major vessels and no significant stenosis as demonstrated on catheterization and CT. Because of its pre-pulmonic course, it would not cause long term morbidity and was managed medically.

Discussion: Coronary angiography best determines the extent of CAD. Cardiac CTA is superior in determining the anatomical course of the anomalous coronary artery. Our patient demonstrated a pre-pulmonic course of LAD and was treated medically.



Image#1
A) Left aortic sinus angiogram revealing no left main coronary artery (AP projection); B) Engagement of the right coronary artery revealing the anomalous LCx arising off of the proximal vessel (AP); C) Selective engagement of the anomalous LAD arising from the roof of the proximal RCA (LAO 30°); D) Partial engagement of the right coronary system, demonstrating a single large trunk that arose from the right aortic sulcus and gave way to the three main coronary arteries (LAO 30°)

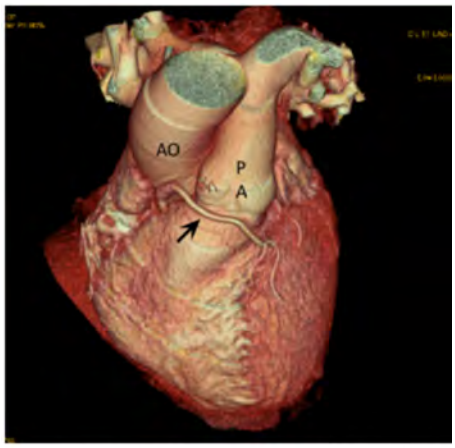


Image 2: three dimensional construction of Cardiac CT demonstrating the pre-pulmonic course of the LAD

Ref. 1)Angelini P. Coronary artery anomalies--current clinical issues: definitions, classification, incidence, clinical relevance, and treatment guidelines. Tex Heart Inst J 2002;29:271-8
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13.Broken Heart Syndrome After a Stolen Car

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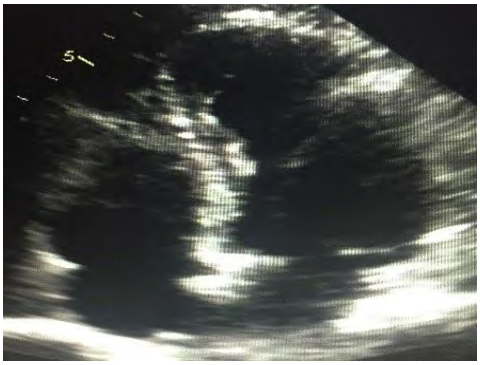
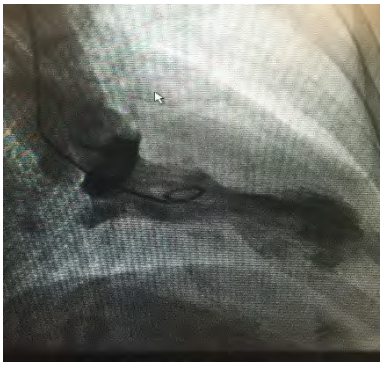
***Drexel University College of Medicine: Internal Medicine

Introduction: Stress cardiomyopathy (also called apical ballooning syndrome, takotsubo cardiomyopathy, broken heart syndrome, and stress-induced cardiomyopathy) is a syndrome characterized by transient regional systolic dysfunction of the left ventricle (LV), mimicking myocardial infarction, but in the absence of angiographic evidence of obstructive coronary artery disease or acute plaque rupture.

Case Discussion: The patient is 65-year-old Caucasian female with PMH only significant for HTN presented to a hospital due to complain of dizziness along with chest discomfort. On further history, it was found out that Patient was in lot of emotional stress from past 1 hour because she was looking for her stolen car which she parked in a parking lot Initial work up showed troponin peak 3.42 no ischemic changes on EKG, the echo showed LVEF of 40 % but it showed mild to distal endocardium and apex is severely hypokinetic/akinetic. LHC showed clean coronaries but typical apical ballooning consistent with Tajostubo cardiomyopathy. Patient was started on ACE inhibitor and carvedilol and discharge from hospital after 4 days with arrangement for close follow up in Heart failure Conclusion: Stress-induced cardiomyopathy (SIC) causes about 2% of acute coronary syndromes A physical or emotional trigger is often but not always present. In the International Takotsubo Registry study, 15.3 percent of patients with stress cardiomyopathy had concurrent coronary artery disease detected by coronary angiography [1].





Ref. 1. Templin C, Ghadri JR, Diekmann J, et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med 2015; 373:929.
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14.Allergic Heart Attack; Kounis Syndrome Resulting from Intravenous Vancomycin

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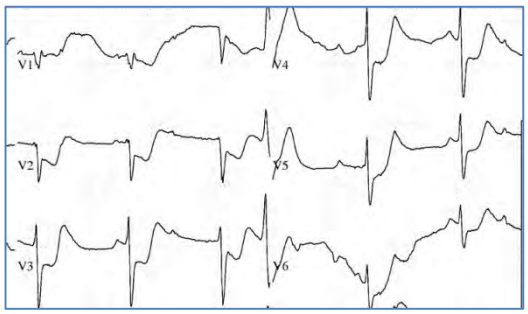
**Abington Memorial Hospital: Department of Medicine, Division of Cardiology

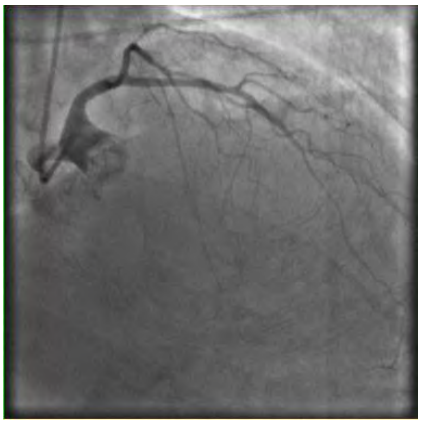
Introduction Acute coronary syndrome association with acute allergic reactions has been recognized forseveral years (Kounis Syndrome). The first reported event occurred in 1950(1). Below is a very interesting case of intravenous vancomycin associated kounis syndrome mimicking as STEMI.

Case: A 72 years old male with past medical history of benign prostate hypertrophy and depression presented to ER with chief complaint of fevers, dysuria and right flank pain. He had a history of chronic indwelling Foley catheter with recent hospitalization for pneumonia. Patient was started on intravenous antibiotics including vancomycin and aztreonam for acute pyelonephritis. Soon after the intravenous vancomycin was started patient started to develop facial flushing and redness (Red Man Syndrome). Also it was noticed that his chest is feeling “heavy”.



EKG was obtained which showed ST segment elevation in leads II, III and aVF and reciprocal depression in leads V1 and V2. PCI alert was activated and patient was taken to cardiac catheterization lab. Surprisingly on cardiac angiogram no coronary artery atherosclerotic disease was seen but vasculature was in diffuse spasm. Patient was given intravenous anti histamine and steroids which resolved the vasculature spasm and patient symptoms abated.

Conclusion: Kounis syndrome is an underdiagnosed entity. Early identification of this syndrome will enable optimal management of patients with both acute allergic and/or myocardial events(2). Additional research, including randomized trials, is needed to better characterize the epidemiology, clinical characteristics, and diagnosis of KS, and to better define appropriate preventive and interventional measures.



Ref. 1) Vivas D, Rubira JC, Ortiz AF, et al. Coronary spasm and hypersensitivity to amoxicillin: Kounis or not Kounis syndrome? Int J Cardiol 2008;128:279–281

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15.West Nile Virus Induced Cardiomyopathy with Left Bundle Branch Block

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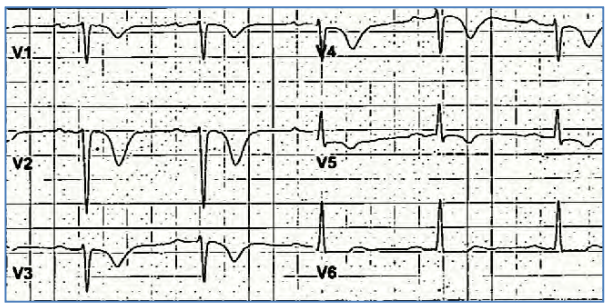
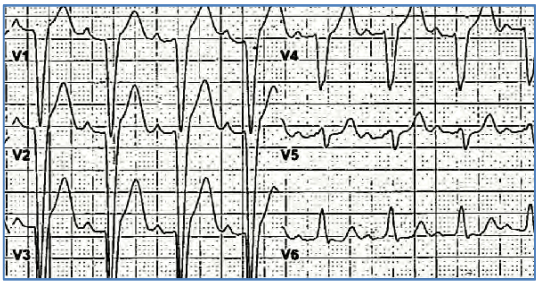
****Drexel University College of Medicine: Department of Medicine, Division of Cardiology

Background: West Nile Virus (WNV) is a mosquito-borne infection first reported in the US in 1999. Approximately 40,000 cases have been documented but WNV infection associated with significant arrhythmias has been rarely reported. .

Case: A 78-year-old man with past medical history of hypertension, syncope status post pacemaker, and a recently treated upper respiratory infection presented with a three-day history of ascending motor weakness. The patient was presumptively diagnosed with Guillain-Barre Syndrome (GBS) and started on plasmapheresis. However, patient's motor weakness worsened and he was intubated for altered mental status and hypoxemia. Cerebrospinal fluid (CSF) studies tested positive for WNV IgG and IgM and he was diagnosed with neuroinvasive WNV infection. After 11 days of supportive care, he was extubated and eventually discharged to inpatient rehabilitation. During hospitalization, the patient developed a new left bundle branch block (LBBB). His troponins peaked at 0.14 and the echocardiography showed an ejection fraction (EF) of 30-35%. Following extubation, repeat electrocardiogram showed persistent LBBB and repeat echocardiography showed an EF of 45-50%. The patient was diagnosed with WNV cardiomyopathy as no other causes could explain the new LBBB with reduced EF.





Discussion: Physicians managing patients with WNV may observe cardiomyopathy with significant arrhythmias such as LBBB. The patient was treated medically with Carvedilol and Losartan for suspected WNV-induced cardiomyopathy. Emergent catheterization was not done due to low suspicion for ischemic etiology. Despite the patient's persistent lower extremity weakness, his stable vital signs and improvement on the repeat echocardiography prompted confidence in outpatient management.

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16.Hemophagocytic Lymphohistiocytosis: Acute Liver Failure in Disguise

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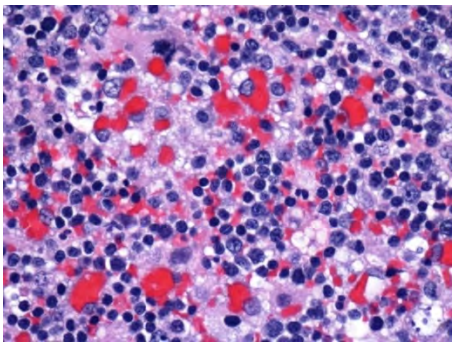
Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a rare but life-threatening syndrome of excessive inflammation and tissue destruction due to abnormal immune activation. **Case**: A 22 year old African American male with a history of schizophrenia presented as a transfer from an outside hospital with intermittent fevers as high as 103.5F, diffuse lymphadenopathy, and bilateral upper extremity pruritic, red, raised rash for 9 days. Initial lab work was significant for elevated transaminitis, but during the hospital course, he clinically decompensated and was transferred to the medical ICU; impending acute liver failure was suspected with spiking fevers, an elevated WBC, and worsening liver function. After viral workup of his hepatic injury was negative, serum LDH and ferritin were ordered, which were significantly elevated at 1900 IU/L and 3300 ng/nl, respectively. A lymph node biopsy was performed, which revealed parafollicular T-cell expansion and increased histiocytes consistent with hemophagocytic lymphohistiocytosis.



He was started on dexamethasone and received IVIG infusions followed by etoposide. As his clinical status and labs improved, he was deemed stable for discharge after completion of 8 weeks of HLH-94 protocol.[1]. **Discussion**:The diagnosis of HLH can be met from molecular evidence or from fullfilling 5 out of 8 criteria; fever greater than 7 days, splenomegaly, cytopenia, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis in bone marrow or lymph node, ferritin > 500 mcg/L, low or absent NK cell activity, or soluble CD25 level > 2400 U/mL [2]. In patients with suspected HLH, immediate diagnosis and treatment is needed to improve survival.

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17.A Rare Case of Bilateral Emphysematous Pyelonephritis

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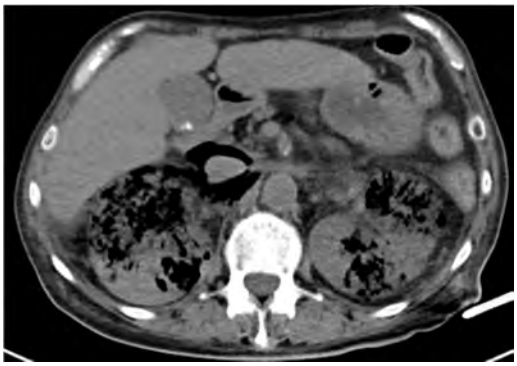
**Drexel University College of Medicine: Department of Medicine, Division of Internal Medicine

Introduction: Emphysematous pyelonephritis (EPN) is a rare, life-threatening condition that occurs primarily in uncontrolled diabetics[1]. **Case**: A 62 year old Caucasian female with a

past medical history of uncontrolled diabetes and alcohol abuse was brought to the ED after being found down by her roommate. Upon arrival she was found to be febrile, hypotensive,with a GCS of 4.She was intubated for airway protection, started on broad spectrum antibiotics, intravenous fluids, and vasopressors. A foley catheter was placed, which revealed necrotic/black urine;a CT abdomen/pelvis was perfomred which showed type 4 bilateral emphysematic pyelonephritis. She was then urgently rushed to the operating room for bilateral ureteral stent placement with the hope of salvaging kidney function.. A bilateral total nephrectomy was discussed with her family;, however decision was made to withdraw support and proceed with comfort measures.

Discussion: EPN is an uncommon condition, however bilateral EPN (10% of EPN cases) is a more rare condition, with an estimated 75% mortality rate with treatment and > 95% mortality without treatment [2].. The pathophysiology behind EPN is unclear, but four factors are involved; gas forming bacteria (E.Coli, Krebsiella Pneumoniae, Proteus Mirabilius, and Pseudomonas Aeruginosa), high tissue glucose, impaired tissue perfusion and immune response [3]. The hallmark of diagnosis and treatment is with CT scan (with staging of 1-4), IV antibiotics, vasopressors and urgent nephrectomy (resulting in dialysis, if bilateral).



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2. Dunn SR, Dewolf WC, Gonzalez R: Emphysematous pyelonephritis: report of 3 cases treated by nephrectomy. J Urol. 1975, 114: 348-50
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18.Bilateral Posterior Fossa Meningiomas: A Possible Case of Neurofibromatosis Type 2

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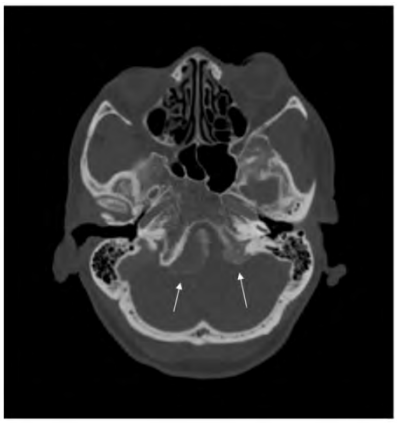
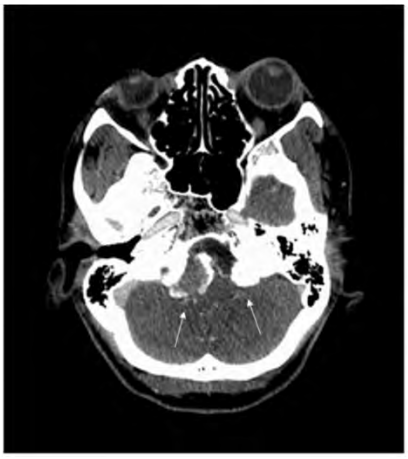
**Drexel University College of Medicine
**Drexel University College of Medicine: Department of Radiology

Introduction: Neurofibromatosis Type 2 (NF2) is an autosomal dominant disorder that usually presents in adolescence to early adulthood with symptoms such as progressive hearing loss and tinnitus. This is due to the development of classic bilateral vestibular schwannomas that are virtually diagnostic of NF2. Other tumors of the central nervous system are often present and include tumors such as schwannomas of other cranial nerves, meningiomas, gliomas, and ependymomas (1). .

Case: We present an unusual case of incidentally found bilateral meningiomas at the cerebellopontine angles in a 73 year old African American female who presented with fever and altered mental status. She did not carry a

prior diagnosis of NF2, but was one month status post sub-occipital craniotomy for partial resection of a meningioma at the right cerebellopontine angle. During her hospital course the patient was treated empirically for post-operative bacterial meningitis and received multiple head CTs which demonstrated calcified meningiomas in the anterior portion of the posterior fossa as seen in the images. .





Discussion: The patient presented with two classically located cerebellopontine angle meningiomas, with one each identified bilaterally, highly suspicious of NF2. Although the patient lacked presenting symptoms such as hearing loss or tinnitus and further, did not have a positive family history, it was highly recommended clinically that the patient undergo genetic testing for NF2 (2). In general, if NF2 is suspected in a patient, contrast-enhanced MRI imaging of the brain and spinal cord should be conducted to search for schwannomas, meningiomas and other NF2-related tumors.

Ref. 1. Ardern-Holmes S, Fisher G, North K. Neurofibromatosis Type 2: Presentation, Major Complications, and Management, With a Focus on the Pediatric Age Group. Journal of Child Neurology. 2016;32(1):9-22.
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19.A Rare Case of Tension Hydropneumothorax from Disseminated Endometriosis

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**Drexel University College of Medicine: Department of Medicine, Division of Internal Medicine

Introduction: Tension hydropneumothorax is a form of pneumothorax involving both air and fluid within the pleural cavity, leading to increased intra-thoracic pressure and a shift in mediastinal structures to the contralateral side. The most common etiologies are iatrogenic, infectious, and trauma-related.

Case: A 34 year old African American female presented to the emergency department with dyspnea on exertion, abdominal distention, 10-pound weight loss, and constipation. Upon presentation, she was tachycardic, in respiratory distress, with an oxygen saturation of 92% on room air; on physical exam, she had absent breath sounds in her right lung fields, and abdominal distention with shifting dullness. A CT Chest/Abdomen/Pelvis showed a large right pleural effusion with a shift in her mediastinal structures to the left, pelvic lymph node enlargement, multiple soft tissue masses in the bladder, liver, and ovaries, and significant amount of ascites. A thoracentesis was

performed, draining a large amount of blood; cytology was negative for malignancy. After the procedure, the pneumothorax persisted, which suggested the diagnosis of tension hydropneumothorax. A thoracostomy tube was inserted, which led to improvement of her symptoms. A biopsy of the lymph node revealed endometriosis. OBGYN was consulted, and recommended the patient be started on progesterone injections. After the chest tube was removed, she was stable to discharged with close follow up with gynecology.

Conclusion: Thoracic manifestations of disseminated endometriosis (DE) are rare but include pneumothorax. To our knowledge, there has only been one documented case of DE causing a tension hydropneumothorax, as in our patient.

Ref. 1. Jubanyik KJ, Comite F. Extrapelvic endometriosis. Obstet Gynecol Clin North Am 1997; 24:411.
2. Bagan P, Berna P, Assouad J, et al. Value of cancer antigen 125 for diagnosis of pleural endometriosis in females with recurrent pneumothorax. Eur Respir J 2008; 31:140.
3. Vinatier D, Orazi G, Cosson M, Dufour P. Theories of endometriosis. Eur J Obstet Gynecol Reprod Biol 2001; 96:21.
4. Alifano M, Jablonski C, Kadiri H, et al. Catamenial and noncatamenial, endometriosis-related or nonendometriosis-related pneumothorax referred for surgery. Am J Respir Crit Care Med 2007; 176:1048.
5. Rousset-Jablonski C, Alifano M, Plu-Bureau G, et al. Catamenial pneumothorax and endometriosis-related pneumothorax: clinical features and risk factors. Hum Reprod. June 16 2011
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20.New Black Box Warning for Lorazepam

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**Abington Memorial Hospital: Department of Medicine, Division of Neurology

Background: Lorazepam is a benzodiazepine with an onset of action within seconds. It is commonly used for a rapid solution for patients in alcohol withdrawal, acute seizures, and anxiety. Despite its common usage, Lorazepam has many adverse effects. The FDA made a recent announcement regarding "Boxed Warnings" for combined usage of opioids, CNS depressants, and benzodiazepines with increased risk of sudden deaths.

Case: A 68-year-old male patient with a past medical history of glioblastoma status post resection and on Temozolomide presented to the hospital after he was found on the bathroom floor in a confused state. In the ER, he was neither responding to questions nor following commands. The patient was started on IV fluids and loaded with Levetiracetam. While being examined by the medical staff, the patient started experiencing tonic-clonic movements in all four extremities. He was given 2 mg of intravenous Lorazepam and within seconds went into asystole on telemetry. Chest compressions were started immediately and he eventually had the return of spontaneous circulation within minutes. The patient was further monitored in the ER and his mental status gradually returned back to his baseline. He was eventually examined by cardiology prior to being admitted. .

Discussion: In light of the FDA's warning, should Lorazepam be used more judiciously for a patient currently on a CNS depressant such as

Temozolomide?

Ref. 1. FDA News Release: FDA requires strong warnings for opioid analgesics, prescription opioid cough products, and benzodiazepine labeling related to serious risk and death from combined use. US Department of Health and Human Services. Webpage. 2016.

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21. Linagliptin Induced Acute Pancreatitis

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*Mercy Health System: Internal Medicine
**Mercy Health System: Department of Medicine

Introduction: We report a rare case of acute pancreatitis in a patient on Linagliptin, which is well described side effect of the Dipeptidyl peptidase - 4 (DPP-4) inhibitors as a class. However, there are only very few reported cases of Linagliptin related pancreatitis.
Case: Fifty three year old lady with history of HIV, DM and Hepatitis C, who was on Dolutegravir, Emtricitabine/Tenofovir, Ledipasvir/Sofosbuvir, Insulin and Linagliptin. She presented with acute onset epigastric pain and nausea, with epigastric tenderness on physical exam. Elevated lipase of 1137 U/L raised the suspicion of acute pancreatitis which was confirmed with a CT scan of the abdomen that showed peripancreatic stranding and retroperitoneal fluid. Other common causes of acute pancreatitis were ruled out such as alcoholism, hypertriglyceridemia or biliary disease. After discontinuation of Linagliptin and Antiretroviral therapy (ART), her lipase levels trended down with clinical improvement. Subsequently her ART was resumed without any symptoms or rise in the lipase levels.
Discussion: All incretin based therapies have been associated with the risk of pancreatitis based on initial clinical trials and subsequently post-marketing analysis. In fact, FDA issued a warning regarding Linagliptin and pancreatitis. (1) A large meta-analysis of the incretin based therapies and their association with pancreatitis, showed that previously implicated high risk in unfounded. (2) Meta-analysis from 22 placebo controlled studies showed only 2 cases of acute pancreatitis and 3 cases of chronic pancreatitis. (3) Our case signifies that Linagliptin can cause acute pancreatitis.

Ref. 1.
http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm319215.htm
2. Giorda B et al: Incretin-based therapies and acute pancreatitis risk: a systematic review and meta-analysis of observational studies. Endocrine (2015) 48:461–471
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22.The Dizzying DKA: a unique presentation of euglycemic diabetic ketoacidosis secondary to SGLT-2 inhibitor therapy

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Introduction: SGLT-2 inhibitors have proven to be great medications to achieve glycemic control in diabetic patients, particularly type 2. However, one of the rare side effects of these medications is euglycemic diabetic ketoacidosis (euDKA) (4). Here, we present a case of euDKA

with an atypical presentation. **Case**: A 46 year-old Caucasian male with past medical history of hypertension and type 2 diabetes mellitus presented with 1-day complaint of dizziness and lightheadedness. Patient's review of symptoms was negative. His home medications included Amlodipine-Benazepril, Liraglutide, Nebivolol, Rosuvastatin and Canagliflozin-Metformin. His physical exam and vital signs were unremarkable. Laboratory studies were significant for an anion gap of 19, blood glucose 156, and beta-hydroxybutyrate 19. His urinalysis was positive for glucose and ketones. Ethanol, salicylate, lactic acid and urine drug screen were all within normal limits. Infectious workup was negative. Based on the presentation, euDKA was determined as the most likely diagnosis. Patient's Canagliflozin was stopped and he was given IV fluids. The following day, his symptoms resolved and labs normalized. He was instructed to stop taking Canagliflozin to avoid further episodes. **Discussion**: EuDKA is a rare side effect associated with SGLT-2 inhibitors, occurring in <0.1% of type 2 DM patients (2). EuDKA is pathophysiologically similar to DKA except the SGLT2-induced glycosuria artificially lowers plasma glucose levels and predisposes to increased ketogenesis (3). EuDKA secondary to SGLT-2 inhibitors presents with a wide range of symptoms, hence making clinical identification and diagnosis difficult (4,5). The treatment of choice typically is IV hydration and discontinuation of the SGLT-2 inhibitor.

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3. Palmer BF, Clegg DJ, Taylor SI, Weir MR. Diabetic ketoacidosis, sodium glucose transporter-2 inhibitors and the kidney. Journal of Diabetes and Its Complications. 2016;30:1162-1166.
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5. Rosenstock S, Ferrannini E. Euglycemic diabetic ketoacidosis: A predictable, detectable, and preventable concern with SGLT-2 inhibitors. Diabetes Care. 2015;38:1638-42.

23.Hepatocellular Carcinoma in a Non-Cirrhotic Liver

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**Abington Memorial Hospital: Department of Medicine, Division of Medical Oncology

Case: A 50 year-old man presented with right upper quadrant abdominal discomfort for 3 months. He had nausea, poor appetite, fatigue and unintentionally lost around 20 pounds since. He had a past medical history of degenerative lower back disease and GERD. He had been a lifelong non-smoker, teetotaler and was a former body-builder. ?Family history was negative for cancers. His vitals were stable. On exam, he was notably cachectic, had hepatomegaly with an irregular contour and bilateral pitting pedal edema. His labs were significant for AST 68, ALT 60, ALP 538, with a normal bilirubin, normocytic anemia and hypoalbuminemia. Abdominal ultrasound showed a 17 cm mass in the right liver lobe and triple phase CT showed increased arterial uptake. Hepatitis serologies were negative and AFP was mildly elevated (63). IR-guided biopsy confirmed hepatocellular carcinoma (HCC). The patient was started on sorafenib, a VEGF inhibitor which was stopped prematurely as he

developed hand-foot syndrome. He died within one year of being diagnosed. The patient had admitted to abusing testosterone injections for several years, which was thought to be the underlying cause of his HCC in the absence of other risk factors or underlying cirrhosis.

Discussion: The correlation between anabolic misuse by bodybuilders and the development of HCC has been reported in the literature (1,2). There are now epidemiological, clinical, and experimental observations which suggest that an androgenic environment favours development of HCC (3). Bodybuilders abusing anabolic androgen steroids have a high risk of developing HCC and should be closely monitored.

Ref. 1. Hardt A, Stippel D, Odenthal M, Holscher AH, Dienes HP, Drebber U. Development of hepatocellular carcinoma associated with anabolic androgenic steroid abuse in a young bodybuilder: a case report. Case Reports Pathol. 2012;2012:195607.
2. Solbach P, Potthoff A, Raatschen HJ, Soudah B, Lehmann U, Schneider A, et al. Testosterone-receptor positive hepatocellular carcinoma in a 29-year old bodybuilder with a history of anabolic androgenic steroid abuse: a case report. BMC Gastroenterol. 2015;15:60.
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Medical Essay

The Scourge of Heroin Abuse

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Heroin is creating a growing addiction crisis across the United States. Once considered an urban drug, it has found a new market in small towns and suburbs. Despite efforts to curb this hike in abuse, its overdose and death rates continue to increase. Many addicts trace their problem back to prescription opioids. Heroin becomes a cheaper substitute when they run out of prescriptions or street access. While efforts to reduce availability of prescription opioids have begun to show success, the supply of heroin has been increasing. Whether the availability caused the surge in use or the demand has increased the availability is yet to the determined. Heroin can cause respiratory arrest at high doses especially if co-ingested with other central nervous system depressant especially alcohol, barbiturates and benzodiazepines (1). It is relatively cheaper and more accessible than prescription opioids (2). When used intravenously, there is increased risk of overdosing and exposure to blood-borne diseases such as hepatitis.

The death rate from drug overdose reached a record high in 2014 largely due to opioid analgesics and heroin. Heroin users doubled from 2002 to 2014 (3). Tighter restrictions for prescription opioids led to a reduction in their abuse, but the number of heroin abusers increased (3). This increase seems largely triggered by increasing opioid addiction driven by prescription opioids, and increased heroin supply (4). Strategies to curb this epidemic are directed towards prevention (exposure and availability) and treatment (early identification of at risk populations, acute and chronic therapy). The Opioid Initiative of March 2015

was aimed at reforming prescription practices and expanding access to treatment. Yet fewer addicts receive medication-assisted treatment (MAT). A renewed effort by the FDA February 2016 focuses on collaborations with physicians and pharmaceutical companies to address pain management, development of alternative medications (without addictive properties of opioid) and approaches, and creating a clear guideline for prescribing opioids (5). In March 2016, the Centers for Diseases Control and Prevention released an opioid prescription guideline with emphases on considering non-opioid pain relievers or nonpharmacological options, conducting a urine test before opioid therapy, starting at lowest dose possible, avoiding more than 90 morphine mg equivalents (MME), prescribing immediate-release as opposed to longer-acting opioids, and limiting treatment for acute pain to usually no more than 7 days (6).

On the 7th of July 2016, the Comprehensive Addiction and Recovery Act was signed into law authorizing $181 million towards the course of heroine abuse reduction. It is the first major federal addiction legislation in 40 years and the most comprehensive effort to address the opioid epidemic. It encompasses all six pillars for a coordinated response – prevention, treatment, recovery, law enforcement, criminal justice reform, and overdose reversal. In addition, it creates programs and expands treatment access.

Opioid-related intensive care unit admissions and mortality have risen sharply in recent years. In our center there has been a recent surge in the number of admissions for heroine intoxications with associated death. We had a classic case of a 31-year-old female with a history of hepatitis C virus infection, anxiety and depression, polysubstance abuse including benzodiazepine, cocaine and intravenous heroin addiction. She initially quit after her first rehabilitation but had a rebound when she received a prescription of oxycodone for pain control. She was a divorced mother of three children residing in suburban area. She smoked about a pack of cigarettes per day for over 10 years and drank alcohol socially. She was brought to the emergency room after being found in cardiac arrest in her bathroom with bags of heroin around her. She was successfully resuscitated, and received a total of 2.4 mg of naloxone with no improvement. On arrival, she was unresponsive, pupils fixed, hypo ventilating, hypothermic and hypotensive. She was intubated and started on blood pressure support medications. Arterial blood gases indicated a pH of 6.5, bicarbonate of 13mmol/L, pCO2 of 90 mmHg and lactic acid of 16mmol/L. Her serum drug screen revealed an alcohol level of 54 mg/dl and her urine drug screen was positive for opioids. Computed tomography of her brain showed diffuse cerebral edema with uncal herniation suggestive of hypoxic brain injury. Her cerebral angiogram was without intracranial blood flow. A diagnosis of brain death was made; she was extubated and subsequently expired. This case emphasizes the dangers of heroin abuse and the importance of identification of at risk groups and behaviors.

To summarize, it is important to remember that death from any opioid abuse is preventable and physicians are at the fore front of this. There is an urgent need for identification of at risk individuals, improvement of the treatment capacity for opioid use disorders and reduction

of the supply of illicit opioids, particularly heroin. A comprehensive strategy that balances addressing the misuse of opioids while protecting the rights of individuals in need of pain control should be adopted. It is an effort that will require collaboration between government agencies, healthcare providers, the medical products industry, communities, patients and their families.

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Review Articles

1.Management of Massive Hemoptysis in Post-Chemotherapy Post-Transplant Patient with Extracorporeal Membrane Oxygenation (ECMO)

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Introduction: Extracorporeal Membrane Oxygenation (ECMO) or extracorporeal cardiopulmonary resuscitation (ECPR) has recently been used as a life-saving tool for hypoxic patients and patients with circulatory collapse. There are two types of ECMO, veno-arterial (VA-ECMO) and veno-venous (VV-ECMO). Veno-arterial ECMO is a process in which blood is taken from the venous system (right atrium or vena cava); oxygenated; and returned to the arterial system (femoral, axillary, carotid arteries or ascending aorta). VA-ECMO bypasses both the heart and the lungs and therefore provides both respiratory and hemodynamic support. VV-ECMO is a process in which blood is taken from the venous system, oxygenated, and returned to the venous system. VV-ECMO is used when only oxygenation is needed and hemodynamics are stable. Complications associated with ECMO, such as bleeding, lead to significant morbidity and mortality. Although these complications may be related to the underlying indication for the use of ECMO or directly related to ECMO, ECMO has been gaining popularity as salvage therapy for select patients with refractory cardiopulmonary shock.|This case describes successful use of ECMO/ECPR in a heart transplant patient who developed massive haemoptysis likely secondary to an

opportunistic infection in the setting of an extended period of neutropenia. His neutropenia was the result of chemotherapy treatment for post-transplant lymphoproliferative disorder (PTLD).

Case Presentation: The patient is a 30-year-old Caucasian male with a past medical history of heart transplant for familial non-ischemic cardiomyopathy (5 years prior to presentation) on Tacrolimus who initially began to develop abdominal pain, back pain, fevers, chills and night sweats 3 years post-transplant. Upon development of these B symptoms, diagnostic evaluation was consistent with Epstein Barr Virus (EBV) and Post-Transplant Lymphoproliferative Disorder (PTLD). During the two years between the diagnosis of PTLD and presentation for this case report, the patient had multiple hospitalizations related to the EBV/PTLD.

The patient presented for this hospitalization with a chief complaint of abdominal pain, fatigue, decreased oral intake, and decreased exercise tolerance that had progressively worsened over 2 weeks. The patient had reported measured fevers at home with a maximum of 102 F. The patient was evaluated for these symptoms and was admitted to the Cardiac Care Unit (CCU). Vital signs on admission were temperature 97.7F, heart rate 115 and regular, respiratory rate 20, BP 110/70 and oxygen saturation 94% on room air. Other than minimal hepatomegaly physical examination was unremarkable. Pertinent labs on admission were WBC 6.5, sodium 128, potassium 6.7, BUN 122, creatinine 5.00, and LDH of 17, 360. .

On day 2 of hospitalization, Flow Cytometry was done which showed B-cell Lymphoma and the patient received treatment for lymphoma with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Etoposide, Dexamethasone, and Allopurinol for five treatments. During the next nine days the patients absolute neutrophil count (ANC) trended down from 465 PMNs/uL to <50 PMNs/uL. .

However as the patient's neutropenia began to resolve and patient was being prepared for discharge, the patient developed fever, Tmax 100.8 F and complained of haemoptysis (1-2 teaspoons), therefore his discharge was held (it was felt to be throat irritation/sore throat). The next morning the patient reported feeling better and had not had additional hemoptysis, however, shortly after this observation, the patient developed massive hemoptysis compromising his airway. The patient was intubated and chest X-ray obtained. Chest X-ray showed complete opacification of the left hemithorax. The patient was also noted to be febrile to 103.2F for which Acyclovir, Atovaquone, Vancomycin, and Meropenem (Initially given load of Cefepime) were initiated. The patient acutely declined. The patient had declining hemodynamics and an ominous blood gas demonstrating hypoxia pO2 26/SaO2 26%, hypercapnia with PCO2 160, and acidosis with pH 6.9. Shortly thereafter, the patient had a cardiac arrest for pulseless electrical activity, requiring cardiopulmonary resuscitation. Given the patient's age and likelihood of recovery presumably from invasive infection, the patient was started on VA-ECMO with cannulation in the left femoral vein and right femoral artery as a bridge to recovery. Mechanical ventilation was then changed to rest settings (Respiratory rate <6, FiO2 0.2-0.3, and airway pressures <30/10) for the prevention of ventilator induced lung injury (VILI).

After stabilizing his airway, Pulmonology was consulted for bronchoscopy and tamponade of the left main bronchus as the patient continued to have massive hemoptysis. The bronchoscopy showed complete occlusion of the left main and partial occlusion of the right main bronchus and clots were removed. CT Chest after tamponade would confirm pulmonary arterial hemorrhage with suspected invasive organism. Therefore, Interventional radiology was consulted to embolize the suspected bleeding artery. The diagnostic workup included cultures and stains of the bronchoalveolar lavage. The lavage was negative for organisms, fungal organisms, and PCP. Non-invasive serological markers such as; galactomannan antigen and 1,3-b-glucan were also negative. A lung biopsy for diagnosis of Aspergillosis was considered but deferred due to high risk of bleeding on ECMO. However, given high suspicion for angio-invasive Aspergillosis, anti-fungal treatment with amphotericin B and micafungin was continued. During the treatment of invasive aspergillosis, tacrolimus was discontinued but the patient was maintained on rituximab and steroids during ECMO intervention. .

The patient remained on ECMO for 7 days total. As hemodynamics improved, the patient was switched from VA-ECMO to VV-ECMO. VV-ECMO was discontinued when there was adequate recovery of the lungs. While on ECMO, heparin was used for anticoagulation. However, due to refractory hemoptysis, heparin was discontinued on day 6 of ECMO. Patient remained intubated for 7 additional days after discontinuation of ECMO with intermittent spontaneous breathing trials and 2 re-intubations for hypercapnia. The patient was successfully extubated after 14 days. He showed no signs of neurological deficits during his hospital stay and was successfully discharged home on Posaconazole for treatment of invasive pulmonary Aspergillosis. The patient had disease/symptoms free period that spanned several months before returning to an outside hospital with recurrent PTLD. Unfortunately, within the next several months, patient returned with recurrent B symptoms requiring further Chemotherapy. Eventually, the patient and family opted to receive PTLD treatment at a different outside hospital. While receiving chemotherapy he would again develop pneumonia w/ associated bilateral pleural effusions and similar pulmonary hemorrhage that was treated prophylactically and empirically with antifungals. However, he died from this event. The infectious organism recovered from the outside hospital appeared to have been Stenotrophomonas Maltophilia.

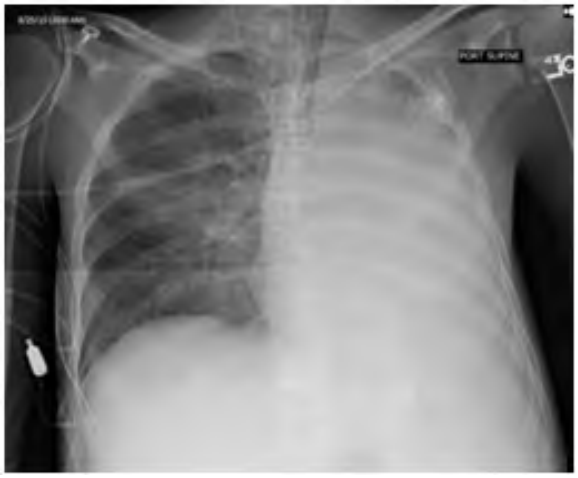

Fig 1 Chest X-Ray after intubation

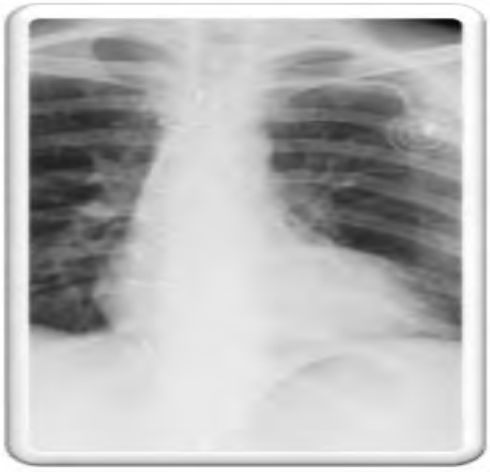

Fig2: Follow-up Chest X-ray 2 months later

Discussion : ECMO is indicated for cardiac and respiratory support or a combination of the two. According to the ELSO Registry reports through January 2015, out of the total 65, 171 patients who received ECLS, 63% of the cases were for respiratory support, 29% for cardiac support and 8% for extracorporeal cardiopulmonary resuscitation (ECPR). Extracorporeal membrane oxygenation (ECMO) refers to modified cardiopulmonary bypass circuit used to provide temporary respiratory or cardiac support. ECMO provides temporary gas exchange, allowing ventilator settings to be reduced to potentially minimize complications of positive pressure ventilation such as barotrauma, volume-related trauma, and oxygen toxicity. There are two types of ECMO, Venoarterial (VA) and Venovenous (VV), in both cases venous blood is removed peripherally via the femoral vein or centrally via cannulation near the right atrium. As in VV-ECMO, the venous blood is returned from the similar source from which is was removed, and in VA-ECMO it is returned peripherally via the femoral artery or centrally via the ascending aorta (2,3,4,6). Whereas in both techniques respiratory support is provided, VA-ECMO in addition only provides hemodynamic support. Clinical trial data supporting use of ECMO in adults is limited, but advancing. Some data suggests that ECMO may reduce mortality when compared to conventional ventilation. Especially in those with primary respiratory indications, 6-month survival without disability was 63% vs 47% (1,5). .

The uses of ECMO are various, Extracorporeal Life Support Organization general guidance for extracorporeal life support is that it is reserved for patients with acute severe heart or lung failure after failure of conventional therapies, indicated with patients with mortality risk >80% and may be considered in those with a mortality risk >50%. Indications for ECMO include hypoxemic respiratory failure with a PaO2/FiO2 < mmHg despite optimization of ventilator settings, hypercapnic respiratory failure with an

arterial pH < 7.20 or Murray score >3.0, ventilator support as bridge to lung transplantation, cardiac transplantation or placement of a ventricular assist device, cardiac failure or refractory cardiogenic shock, massive pulmonary embolism, or failure to wean from cardiopulmonary bypass (3,6,7). The only absolute contraindication to ECMO is a pre-existing condition which is not reversible such as severe neurologic injury or incurable and/or metastatic malignancy; relative contraindications include uncontrolled bleeding, necrotizing pneumonia, high pressure positive pressure ventilation for > 1 week or allograft rejection (3,8,11). .

As our patient required ECMO in the setting of Pulmonary hemorrhage due to an underlying fungal pneumonia and sepsis with a history of heart transplantation, we reviewed the literature regarding ECMO usage in the setting of Pulmonary Hemorrhage, sepsis and transplantation separately in a review.

ECMO and Pulmonary Hemorrhage: As ECMO requires the usage of anticoagulation to prevent thrombus formation within the cardiopulmonary bypass circulation, complications of ECMO can include bleeding, thrombocytopenia, and consumption coagulopathy from both continuous anticoagulation and platelet dysfunction. Bleeding had a complication prevalence of 30-60% per review (9). In a retrospective review of ELSO registry from 1986-2006, pulmonary hemorrhage complication was associated with higher odds ratio of death, 3% vs. 11%, $p < 0.001$ (10). Despite, ECMO usage for many years there is limited evidence in the form of case reports of experience with the use of ECMO in the setting of Pulmonary hemorrhage.

Severe bleeding, although relative, still remains a contraindication to ECMO use. However, in a case series reported by Abrams, four patients with diffuse alveolar hemorrhage (DAH) received ECMO for refractory hypoxemic respiratory failure due to DAH. Etiology of underlying DAH were silicone embolism, Systemic Lupus Erythematous (SLE), granulomatosis with polyangitis, and idiopathic. All four patients received continuous heparin infusions with a goal PTT 40 to 60 seconds and all four survived to decannulation (16). Three of the four patients had heparin without interruption and without adverse bleeding complications, while the fourth had heparin held for 36 hours due to circuit- related thrombotic complications requiring circuit exchange (16).

Furthermore, there have been numerous reports in literature of ECMO and anticoagulation in the presence of pulmonary hemorrhage without the exacerbation of bleeding. In a case of SLE-induced DAH, with the use of systemic anticoagulation, there were no reported hemorrhagic complications (23). Nonetheless, the risk of worsening bleeding is still a major risk factor as seen in a case by Pacheco Claudio where heparin was used to rinse the CVVH circuit. The rinsing of the circuit in a patient with SLE-induced DAH caused significant bleeding (22).

Though bleeding is the most common complication with ECMO (17), ECMO may be considered in the management of patients with severe pulmonary hemorrhage especially with the use of modern ECMO technology for which lower levels of anticoagulation can be used while maintaining patency of the ECMO circuit and minimizing serious adverse bleeding events. Through literature search, most case

reports associated with alveolar or pulmonary hemorrhage were in the setting of Rheumatological diseases such as SLE or autoimmune Vasculitities (16-24). This case proposes that similar concepts for salvage therapy be used in the setting of Stenotrophomonas infections or invasive Aspergillosis causing pulmonary hemorrhage.

Sepsis and ECMO:

Historically, sepsis was a contraindication to ECMO with fears that bacteremia would lead to seeding of the ECMO circuit thus leading to intractable bacteremia. Since the 1990's, several studies have refuted this assumption and now ECMO use during Acute respiratory distress syndrome and septic shock are amongst some of the most common conditions in sepsis that ECMO is used for (12). ECMO's role of salvage therapy can also be indicated in patients with severe sepsis with hypoxemia or inadequate cardiac output which is not supported by conventional therapies. Septic shock has many hemodynamic manifestations; in adults the pattern is with high cardiac output or distributive shock. Although there are no universal criteria to initiate ECMO in this setting, if oxygen delivery cannot be maintained with optimal ventilation, inotropes and IV fluids, then ECMO should be considered. ECMO for sepsis does not appear to be associated with any higher mortality than ECMO use for other conditions. As per ELSO, by 2004 97 of 186 (52%) of patients supported with ECMO for bacterial pneumonia survived (13). In patients with severe left ventricular failure and cardiogenic shock, case reports have suggested possible successful treatment with ECMO (14). In a study by Brechot in 2013, 14 patients received VA-ECMO for refractory cardiovascular failure during bacterial septic shock which was refractory to conventional therapy. These patients previously had no history of left ventricular dysfunction but exhibited severe myocardial dysfunction with LV ejection fraction 10-30% and showing signs of multi-organ failure. 12/14 patients were weaned off the VA-ECMO and 10 patients (71%) were discharged home alive with normal left ventricular ejection fraction and reported good health at 13-month follow up (15).

Transplant:

In a retrospective analysis published in the Journal of Intensive Care Medicine by Tran, the analysis looked at adult patients undergoing VA-ECMO over a 10-year period with 224 cases, it was reported that 35.7% of patients survived to discharge. Those requiring ECMO for heart transplant graft failure had lower mortality compared to other etiologies, 51.6% compared to 69.1% (25). This now brings up the argument of use and efficacy of ECMO in those transplant patients. No literature search was found in the usage of ECMO in previously heart transplanted patients now requiring ECMO for alternative reasons, as we saw in our patient who required ECMO for cardiopulmonary bypass secondary to pulmonary hemorrhage. Transplant recipients are vulnerable to infections because of their immunosuppressive treatments and they can exhibit serious cardiopulmonary dysfunction. In our patient, we found that in his immunocompromised state, he developed pulmonary infections with Aspergillosis and Stenotrophomonas which both likely contributed to his development of pulmonary hemorrhage**.** In a study looking at Kidney transplant recipients during a 4-year period, six of twelve patients who required ECMO, after

cardiopulmonary dysfunction refractory to conventional therapy, were successfully weaned from ECMO. Of the twelve patients, 8 with pneumonia received VV-ECMO, and patients who received VA-ECMO were 1 with pneumonia, 1 case of stress-induced cardiomyopathy due to fungemia and, and 2 cases from septic shock from urinary tract infection or unknown origin. The study showed statistical significance in mortality in those who were severely academic prior to starting ECMO, with survivor mean pH 7.33 and non-survivor mean pH 7.22 (26). .

Extracorporeal life support has also been looked at as a bridge for re-transplantation, particularly lung re-transplantation. In a 2016 study by Hayanga, 854 adult lung re-transplantation for chronic lung allograft dysfunction (CLAD) ranging from 1988 to 2012 were studied in whom 55 (6.8%) on recipients were placed on ECMO as a bridge and 799 (93.2%) of recipients had undergone re-transplantation without the use of ECMO. When comparing the two groups, ECMO patients were more likely to have undergone bilateral lung transplantation, been on mechanical ventilation and been hospitalized in the ICU. ECMO patients also had a significantly shorter waiting time of 6 vs 61 days ($p<0.0001$). When compared to non-ECMO patients, the 30-day survival was higher when compared to the ECMO group 91.2% vs 67.3% (27). CLAD has become a justifiable indication for re-transplantation and ECMO has become the rescue therapy of choice for the bridge to transplantation despite the outcomes in bridged patients is worse when compared to those non-bridged (27). This factor is multifactorial as those requiring ECMO have generally poorer health, are de-conditioned, and require prolonged mechanical ventilation, which in itself can add on numerous further complications for the patient's health.

Conclusion: This case represented a heart transplant patient who had developed PTLD. Because of PTLD, the patient had received further immunosuppression with chemotherapy that resulted in septic shock and pulmonary hemorrhage. Pulmonary hemorrhage and septic shock, though highly morbid as previously discussed, can benefit from ECMO.

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2.Acromegaly: A Case to Question the Use of Somatostatin Analogues.

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Introduction: Acromegaly is a rare disease of hypersecretion of growth hormone. The most common etiology is a growth-hormone (GH) secreting pituitary adenoma, which encompasses 98% of cases(1). Currently, the treatment options for acromegaly consist of neurosurgery, radiotherapy and medical therapy, with somatostatin analogues, dopamine agonists and GH-receptor antagonist, pegvisomant. The most current guidelines recommend surgical therapy as primary treatment and recommend against routine preoperative medical therapy (7).
Case: A 49-year-old African-American male

presented to the Endocrine office for consultation for acromegaly. He presented to an outside hospital for elevated blood glucose and had a prolonged hospital course including diabetic ketoacidosis (DKA), bacteremia, fungemia, and airway edema resulting in tracheostomy. During his admission, he had clinical features suspicious for acromegaly with an elevated insulin-like growth factor 1 (IGF-1) and an MRI that showed a pituitary macroadenoma with suprasellar extension, measuring 2.1 x 2.5 x 1.4 cm. There was mass effect on the anterior optic chiasm and the mass abutted the cavernous internal carotid arteries bilaterally. He was advised to follow-up as an outpatient for care of the acromegaly after discharge. Endocrine history was obtained 5 months after his discharge from the hospital. He denied increase in glove, ring or shoe size. He stated that he was always been tall, even as a child, and reached his current height at age 17. His only prior medical history was type 2 diabetes and hypertension. He was diagnosed with type 2 diabetes 6 years ago and was initially on oral medications. He was on pre-mixed insulin for 20 days after recent hospitalization for DKA. He stopped the pre-mixed insulin on his own and restarted metformin. Patient denied change in weight or difficulty controlling blood pressure when on medication. He denied decreased libido and denied erectile dysfunction. He does not have children, but has never tried to conceive. He denied any visual changes; there was no loss of peripheral vision or visual disturbance. Physical exam revealed blood pressure 158/110, pulse 60, height 6 feet 1 inch, and weight 244 lbs. He had coarse enlarged facial features with a deep voice and large hands and feet. Laboratory studies confirmed an IGF-1 level of 1000 ng/ml (normal 67-205 ng/ml). He underwent a 75 gram glucose suppression test for growth hormone (nadir GH), which resulted in serum growth hormone at 2 hours of 40.3 ng/ml. Other laboratory results were prolactin 15.2 ng/mL (4-15.2), ACTH 18.8 pg/mL (7.2-63.3), cortisol 2.2 ug/dL (2.3-19.4), TSH 1.57 uIU/mL (0.45-4.5), Free T4 1.4 ng/dL (0.82-1.77), FSH 11.1 mIU/mL (1.5-12.4), LH 4.9 mIU/mL (1.7-8.6).

The initial step in treatment is evaluation for surgical removal of the tumor, but in this case, pretreatment with somatostatin analogues was considered because of several features. First, he had a very elevated level of IGF-1and large tumor size. Both high preoperative IGF-1 and pituitary macroadenoma have lower rates of surgical cure (1). Pretreatment with somatostatin analogues could decrease the level of IGF-1 and size of the pituitary macroadenoma to potentially increase the surgical cure rate. He also had a history of tracheostomy for airway obstruction likely secondary to macroglossia during his recent hospitalization. Somatostatin analogues (Octreotide LAR) have been shown to improve respiratory function, as they can reduce soft tissue swelling and decrease sleep apneic episodes by 28-50%(12.). .

Discussion: Acromegaly is a condition of hypersecretion of growth hormone or growth-hormone releasing hormone. Most cases occur as a result of a pituitary macroadenoma; only 10% of GH secreting adenomas are diagnosed as microadenomas (2). The incidence is 5 cases per million per year and the prevalence is 38 to 80 cases per million. The mean age at diagnosis is 40 years (9). Acral and soft tissue proliferation lead to coarsening of the facial

features, such as frontal skull bossing as well as increase in size of hands, lips and nose. Laryngeal mucosal and cartilage hypertrophy can lead to sleep apnea and jaw protrusion. Airway obstruction can also occur as a consequence of macroglossia and laryngeal mucosal and cartilage hypertrophy (2). Tissue and bone overgrowth leads to carpal tunnel or arthralgias and may progress to degenerative arthritis. Biventricular hypertrophy is the most common cardiac manifestation. Cardiovascular disease is the leading cause of mortality followed by respiratory disease and cerebrovascular disease (6).

Diagnosis: Initially, IGF-1 is obtained to screen patients. If IGF-1 is elevated, a nadir serum growth hormone should be evaluated 2 hours after a 75 gram oral glucose load. A nadir serum growth hormone of greater than 1 µg/L indicates growth hormone hypersecretion. Random growth hormone measurement is not recommended secondary to the episodic growth hormone secretion from normal pituitary as well as pituitary adenomas. Once biochemical testing is positive, a pituitary MRI is indicated to evaluate for pituitary adenoma (7).

Treatment: The initial step for treatment of Acromegaly has been transsphenoidal surgery (TSS) to remove the pituitary adenoma followed by repeat transsphenoidal treatment or medical treatment if surgical cure is not achieved after the initial surgery (7). Cure rates after surgery are 80-90% for microadenomas and 50-60% for macroadenomas (7). The surgical cure rates outside of international reference centers is low or unknown. Surgical cure results vary based on preoperative serum GH and IGF-1 levels, tumor invasiveness and the skill of the neurosurgeon (3). Medical therapy is recommended for patient who have persistent disease and have failed surgery or cannot undergo surgical resection (7). Somatostatin analogues (SSA) bind to somatostatin receptors (SSTR) on the surface of somatotroph cells and inhibit growth hormone secretion and/or cell proliferation (9). Medications such as octreotide, lanreotide and pasireotide, have been shown to normalize IGF-1 and improve soft tissue swelling, thus they are first-line agents for the medical therapy of acromegaly. Biochemical control, defined as suppressed GH < 2.5 µg/L and normalization of IGF-1, is achieved in approximately 65% of patients who received SSA after surgery (2). Side effects of somatostatin analogues include abdominal cramps, flatulence and gallstones (7). Pegvisomant is a GH-antagonist that competes with endogenous GH for binding at receptors and block peripheral production of IGF-1. It does not target the pituitary tumor, thus does not decrease GH hypersecretion. Early studies showed dose-dependent normalization of IGF-1 was achieved in 95% of patient who received up to 40 mg daily (7). It is useful in patients who are resistant to SSA, and is considered second-line medical therapy for acromegaly. A surveillance study showed that IGF-1 was controlled in 63% of patients; these results could reflect compliance challenges and inadequate dose titration (7). In theory, the loss of IGF-1 negative feedback to control tumor proliferation can cause rebound mass expansion. In reality, rebound mass expansion rarely occurs and may be as a result of discontinuing SSA (6). Side effects for pegvisomant are nausea, diarrhea, and abnormal liver function tests (9). Dopamine agonists, such as cabergoline and bromocriptine, also suppress growth hormone

and are useful for patient with mild disease. It is useful for modest elevation of GH and IGF-1. It has limited efficacy in the treatment of acromegaly because response to cabergoline decreases over time (7). Stereotactic radiotherapy with delivery of high-energy protons versus gamma knife, CyberKnife or linear accelerator is recommended for the treatment of residual tumor after surgery or if medical therapy is unavailable, unsuccessful or the patient is unable to tolerate the medications. Remission rates after radiotherapy range from 10-60%; it may take many years to see the full therapeutic effect of radiotherapy (7). Hypopituitarism occurs in greater than 50% of patient who underwent radiotherapy within 5-10 years.

Consideration of Medical Therapy before Surgery: There may be a role for pretreatment with somatostatin analogs prior to surgery to improve the surgical outcome for acromegaly. SSA have high efficacy and only approximately 20% of patient have a poor response or resistance (11). Treatment with SSA may cause shrinkage of a GH-secreting pituitary adenoma and in theory may improve the likelihood of radical resection, if given preoperatively. SSA may soften the tumor parenchyma, thus facilitating tumor removal (1). These medications have been shown to control tumor growth in most patients and significantly reduce tumor size in approximately 40-66% of primarily treated patients (11). However, somatostatin analogues are not currently FDA approved for preoperative use in acromegaly. The research investigating the use of preoperative SSA in patient with acromegaly has been conflicting. The preoperative octreotide treatment of acromegaly (POTA) study published in 2008 found overall cure rates in macroadenomas tripled in octreotide pre-treated patients versus patient who did not receive octreotide preoperatively; 50% versus 16%, respectively (3). In a study by Carlsen et al. (3), approximately 33% of patients had biochemical remission after 6 –month treatment with octreotide prior to surgery. Lower preoperative IGF-1 level correlate to lower early postoperative IGF-1 levels, which is a good predictor of long-term treatment response. Preoperative treatment with SSA has been shown to decrease the IGF-1 levels with a mean reduction of 36.5% (3). A study by Bacigaluppi et al. observed that pre-treated patients developed post-surgical hypopituitarism less often compared to non-pre-treated patients, 7.5% and 28.5% respectively (1). A meta-analysis which included four studies and a pool of 261 patients that found that patients who received SSA at least 3 months before TSS had a 22% lower risk of needing medical treatment 3 months post-operatively than patient who went directly to surgery (relative risk 2.15 95% CI 1.39, 3.33) (10). Only one study included in the meta-analysis by Nunes et al. evaluated patients at 6 months and 12 months postoperative. The results favored the use of preoperative SSA at 6 months but there was no difference in remission rates at 12 months. Another study investigated the long-term results of the POTA study, 1 to 5 years after surgery, and did not find a significant impact of preoperative treatment of macroadenomas (5). However, when the data was pooled in with another long-term study, there was a benefit of pretreatment in macroadenomas (5). Another meta-analysis and found that the use of preoperative SSA in GH-secreting pituitary macroadenomas led to improvement in surgical results and was also

cost-effective, but in surgical centers that did not have optimal post-surgical results (11). Patients who had surgery at large surgical center with significant surgical expertise did not benefit from preoperative treatment with SSA (11). In a meta-analysis looking at surgical centers without optimal surgical results, a cost analysis found that preoperative treatment with SSA of GH-secreting pituitary macroadeomas was highly cost effective, with Incremental Cost Effectiveness Ratio (ICER) per patient/year, one decade after surgery of $10512 for SSA (8). Please note that €9973 was converted from Euro to US dollars using current exchange rate as of 12/9/2016; the comparison of cost for medications is difficult because medications have a higher cost in the United States compared to Spain. Along with the potential for improved post-operative outcomes, SSA's may help with respiratory status and improve soft tissue swelling (12). As noted in our case, the patient had respiratory complications related to macroglossia during his recent hospitalization. A tracheostomy had been placed, and was kept in place in anticipation of his upcoming transsphenoidal surgery; intraoperative or postoperative airway obstruction was a concern. Pre-operative SSA treatment in this patient was suggested as it could help to reduce soft tissue swelling and have a beneficial effect on his respiratory status. .

Conclusion: We attempted to get SSA prior to initial transsphenoidal surgery for our patient, but his insurance denied our request because his plan does not allow coverage for SSA if the patient has not had inadequate response to surgery or radiotherapy or if there is not an indication to avoid surgical resection. He was seen by otolaryngology prior to surgery and they also advised to keep the tracheostomy in place until after surgery for airway protection. He underwent initial transsphenoidal surgery to remove the pituitary macroadenoma with Neurosurgery. His postoperative course was uncomplicated and there was no evidence of diabetes insipidus or hypopituitarism. His labs 1 week postoperative were as follows: 8 AM cortisol 18.7 ug/dL, free T4 1.30 ng/dL and serum sodium 140 mmol/L. Three-months after transsphenoidal surgery, he had nadir Growth hormone of 34.3 ng/mL after 75-gram of glucose and repeat IGF-1 was 898 ng/mL, which indicated that he did not have surgical cure. Repeat MRI of the brain showed decreased craniocaudal size of the pituitary lesion; the lesion measured 1.9 x 2.1 x 1.5 cm compared to 1.9 x 2.0 x 2.6 cm on the prior MRI.

Six weeks after initial TSS, he underwent ethmoidectomy, sphenoidectomy and partial septum resection then had repair of glottis stenosis 1 week later. His tracheostomy dislodged twice after repair of glottis stenosis, however, his airway was stable and patent and did not require replacement after the 2nd dislodgement. He underwent a second TSS for removal of pituitary macroadenoma, which resulted in an intraoperative CSF leak, which resolved prior to discharge. Labs drawn 1 week postoperative indicated hypogonadotropic hypogonadism as a complication of surgery. His 8 am cortisol 1 week postoperative was 10.2 ug/dL. He has not had a follow-up IGF-1 since his repeat surgery. Our patient had a large macroadenoma and very high IGF-1 level prior to his first surgery. Thus, the question remains would he have achieved a better outcome and biochemical control after the first TSS if he received preoperative SSA?

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